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## (54) Title: METHODS FOR TREATING GENETICALLY-DEFINED PROLIFERATIVE DISORDERS WITH HSP90 INHIBITORS

Types of Alteration	Background Literature	Affected Genes	Protein Domain	Fusion Protein	Disease
q9, 22(q34; q11)	de Klein, A. et al. Nature 300, 705-707 (1982)	<i>CADL</i> (9q34) <i>BCR</i> (22q11)	cytosine kinase serine kinase	serine + tyrosine kinase	CML/ALL
xiv14 (q11; q22)	Bier, R., Chen, K.-C., Smith, S. D. & Rabbitts, T. H. Cell 43, 703-713 (1985); Derany, C. T. et al. Nature 330, 549-551 (1986)	<i>TCR-α</i> (14q11) <i>Vic</i> (14q32)	TCR- $\alpha$ lg V $\alpha$	Vic-TCR- $\alpha$	T/B-cell lymphoma
q1, 19(q13; p13)	Kimpas, M. P., Moore, C., Sun, X.-H. & Baltimore, D. Cell 60, 547-555 (1990); Naor, J. et al. Cell 60, 535-545 (1990)	<i>PBX1</i> (14q23) <i>E2A</i> (19p13)	HD	AD + HD	pre-B-ALL
11p19(q22; p13)	Hunger, S. P., Olayinski, K., Toyama, K. & Cleary, M. L. Genes Dev. 6, 1608-1620 (1992); Kishu, T. et al. Science 257, 531-534 (1992)	<i>HLF</i> (17q22) <i>E2A</i> (19p13)	bZIP	AD + bZIP	pre-B-ALL
11p15 (q11-q12)	Gilland, E. F. & Solomon, F. Sem. Cancer Biol. 4, 359-368 (1993)	<i>PM1</i> (15q21) <i>RARA</i> (17q21)	Zinc-finger Retinoic acid receptor- $\alpha$	Zinc-finger + RAR DNA and ligand binding	APL
q11, 17(q23; q21)	Chen, Z. et al. EMBO J. 12, 1161-1167 (1993)	<i>FLZ1</i> (11q23) <i>RARA</i> (17q21)	Zinc-finger Retinoic acid receptors	Zinc-finger + RAR DNA and ligand binding	APL
16; 13(q21; q23)	Dybalski, M. et al. Nature Genet. 2, 113-118 (1992); Gu, Y. et al. Cell 71, 791-798 (1992)	<i>MLL</i> (11q23) <i>APF</i> (16q21)	A-T hook/Zn-finger Src-Pro-rich	A-T hook + (Src-Pro)	ALL/pre-B-ALL ALL/pre-B-ALL ALL
18; 11(q21; q23)	Nakamura, T. et al. Proc. Natl. Acad. Sci. U.S.A. 90, 4631-4635 (1993); Lida, S. et al. Oncogene 8, 3085-3092 (1991)	<i>MLL</i> (11q23) <i>APMLL1</i> (19p22)	A-T hook/Zn-finger Src-Pro-rich	A-T hook + (Src-Pro)	ALL/pre-B-ALL ALL ALL
11; 19(q23; p13)	Thiack, D. C., Kohler, S. & Cleary, M. L. Cell 71, 691-700 (1992); Yamamoto, K. et al. Oncogene 8, 2617-2625 (1993)	<i>MLL</i> (11q23) <i>ENL</i> (19p13)	A-T hook/Zn-finger Src-Pro-rich	A-T hook + Src-Pro	pre-B-ALL T-ALL ALL

(57) Abstract: The invention relates generally to methods of treating cell proliferative diseases with HSP90 inhibitors and, depending on the specific aspect and embodiment(s) claimed, to the treatment of proliferative diseases that are associated with fusion proteins, e.g., bcrabl, or mutant proteins or cellular protein isoforms, e.g., mutant forms of p53.



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## Methods for Treating Genetically-Defined Proliferative Disorders with HSP90 Inhibitors

### Field of the Invention

The field of the invention relates to chemotherapeutic treatments of proliferative disorders, including rheumatoid arthritis and neoplasias.

### Background of the Invention

The following description includes information that may be useful in understanding the present invention. It is not an admission that any of the information provided herein is prior art, or relevant, to the presently claimed inventions, or that any publication specifically or implicitly referenced is prior art.

The eukaryotic heat shock protein 90s (HSP90s) are ubiquitous chaperone proteins that are involved in folding, activation and assembly of a wide range of proteins, including key proteins involved in signal transduction, cell cycle control and transcriptional regulation. HSP90 proteins are highly conserved in nature (see, e.g., NCBI accession # P07900 (SEQ ID NO: 318) and XM 004515 (SEQ ID NOs: 319 and 320) (human  $\alpha$  and  $\beta$  HSP90, respectively), P11499 (SEQ ID NO: 321) (mouse), AAB23369 (SEQ ID NO: 322) (rat), P46633 (SEQ ID NO: 323) (chinese hamster), JC1468 (SEQ ID NO: 324) (chicken), AAF69019 (SEQ ID NO: 325) (fleshfly), AAC21566 (SEQ ID NO: 326) (zebrafish), AAD30275 (SEQ ID NO: 327) (salmon), AAC48718 (SEQ ID NO: 328) (pig), NP 015084 (SEQ ID NO: 329) (yeast), and CAC29071 (SEQ ID NO: 330) (frog).

Researchers have reported that HSP90 chaperone proteins are associated with important signaling proteins, such as steroid hormone receptors and protein kinases, including many that are implicated in tumorigenesis, e.g., Raf-1, EGFR, v-Src family kinases, Cdk4, and ErbB-2 (Buchner J., 1999, *TIBS*, 24:136-141; Stepanova, L. *et al.*, 1996, *Genes Dev.* 10:1491-502; Dai, K. *et al.*, 1996, *J. Biol. Chem.* 271:22030-4). *In vivo* and *in vitro* studies indicate that certain co-chaperones, e.g., Hsp70, p60/Hop/Sti1, Hip, Bag1, HSP40/Hdj2/Hsj1, immunophilins, p23, and p50, may assist HSP90 in its function (Caplan, A., 1999, *Trends in Cell Biol.*, 9: 262-68).

Ansamycins are antibiotics derived from *Streptomyces hygroscopicus* which are known to inhibit HSP90s. These antibiotics, e.g., herbimycin A (HA) and geldanamycin (GM), as well as other HSP90 inhibitors such as radicicol, bind tightly to an N-terminal pocket in HSP90 (Stebbins, C. *et al.*, 1997, *Cell*, 89:239-250). This pocket is highly conserved and has weak

homology to the ATP-binding site of DNA gyrase (Stebbins, C. *et al.*, *supra*; Grenert, J.P. *et al.*, 1997, *J. Biol. Chem.*, 272:23843-50). ATP and ADP have been shown to bind this pocket with low affinity, and HSP90 itself has been shown to have weak ATPase activity (Proromou, C. *et al.*, 1997, *Cell*, 90: 65-75; Panaretou, B. *et al.*, 1998, *EMBO J.*, 17: 4829-36). *In vitro and in vivo* studies have demonstrated that occupancy of the N-terminal pocket of HSP90 by ansamycins and other inhibitors alters HSP90 function and inhibits client protein folding. At high concentrations, ansamycins and other HSP90 inhibitors have been shown to prevent binding of client protein substrates to HSP90 (Scheibel, T., H. *et al.*, 1999, *Proc. Natl. Acad. Sci. U S A* 96:1297-302; Schulte, T. W. *et al.*, 1995, *J. Biol. Chem.* 270:24585-8; Whitesell, L., *et al.*, 1994, *Proc. Natl. Acad. Sci. U S A* 91:8324-8328). Ansamycins have also been demonstrated to inhibit the ATP-dependent release of chaperone-associated protein substrates (Schneider, C., L. *et al.*, 1996, *Proc. Natl. Acad. Sci. U S A*, 93:14536-41; Sepp-Lorenzino *et al.*, 1995, *J. Biol. Chem.* 270:16580-16587), and some of these substrates have been shown to be degraded by a ubiquitin-dependent process in the proteasome (Schneider, C., L., *supra*; Sepp-Lorenzino, L., *et al.*, 1995, *J. Biol. Chem.*, 270:16580-16587; Whitesell, L. *et al.*, 1994, *Proc. Natl. Acad. Sci. U S A*, 91: 8324-8328).

This substrate destabilization occurs in tumor and nontransformed cells alike and has been shown to be especially effective on a subset of signaling regulators, *e.g.*, Raf (Schulte, T. W. *et al.*, 1997, *Biochem. Biophys. Res. Commun.* 239:655-9; Schulte, T. W., *et al.*, 1995, *J. Biol. Chem.* 270:24585-8), nuclear steroid receptors (Segnitz, B., and U. Gehring. 1997, *J. Biol. Chem.* 272:18694-18701; Smith, D. F. *et al.*, 1995, *Mol. Cell. Biol.* 15:6804-12), *v-src* (Whitesell, L., *et al.*, 1994, *Proc. Natl. Acad. Sci. U S A* 91:8324-8328) and certain transmembrane tyrosine kinases (Sepp-Lorenzino, L. *et al.*, 1995, *J. Biol. Chem.* 270:16580-16587) such as EGF receptor (EGFR) and Her2/Neu (Hartmann, F., *et al.*, 1997, *Int. J. Cancer* 70:221-9; Miller, P. *et al.*, 1994, *Cancer Res.* 54:2724-2730; Mimnaugh, E. G., *et al.*, 1996, *J. Biol. Chem.* 271:22796-801; Schnur, R. *et al.*, 1995, *J. Med. Chem.* 38:3806-3812). The ansamycin-induced loss of these proteins leads to the selective disruption of certain regulatory pathways and results in growth arrest at specific phases of the cell cycle (Muise-Heimericks, R. C. *et al.*, 1998, *J. Biol. Chem.* 273:29864-72), and apoptosis of cells so treated (Vasilevskaia, A. *et al.*, 1999, *Cancer Res.*, 59:3935-40).

Growth arrest of this sort, provided it can be made selective, has important ramifications for the treatment of certain proliferative disorders, including cancer. Whereas cancer treatments have thus far been limited to traditional surgical removal, radiation, and/or chemotherapy, and

whereas these procedures have been more or less successful, a need remains to develop additional therapies with increased efficacy and decreased side-effects that can be used alone or in combination with existing therapies. There particularly remains a need for cancer treatments that target specific cancer types. The present invention satisfies these needs and provides related advantages as well.

### Summary of the Invention

Applicants report that many proliferative disorders are associated with aberrant proteins that exhibit a dependence on HSP90. In some cases this dependence manifests as a heightened sensitivity to HSP90 inhibitors such that affected cells can be selectively treated using a dosage that is effective against the aberrant cells but which is ineffective or less effective against normal cells. The aberrant proteins may also exhibit increased proteasome-dependent degradation when in the presence of HSP90 inhibitors. While the invention is not limited by mechanism, increased dependence, sensitivity, and /or disposition to preferential degradation may advantageously be used to treat corresponding proliferative diseases according to the methods of the invention.

Among others, the invention targets two groups of aberrant proteins in particular and the corresponding proliferative disorders they are associated with. Within the first group are fusion proteins generated as a result of non-random chromosomal aberrations (such as translocations, deletions and inversions) that juxtapose parts of the coding sequences of two normal cellular proteins (Rabbitts, T., 1994, *Nature* 372:143-149). Duplication of genetic material within a chromosome resulting in a augmented or semi-duplicative transcripts is also a possibility. Within the second group are mutants and isoforms of cellular proteins that override, dominate, or otherwise obscure the natural gene products and their function. For example, mutants and isoforms of p53 family proteins and other tumor suppressor gene products can act as dominant-negative inhibitors of the corresponding normal protein in heterozygous tumor cells (Blagosklonny, M., *et al.*, 1995, *Oncogene*, 11:933-939. Other examples include virally-encoded species of certain kinases, such as v-src and other dominantly-acting mutant oncogene products (Uehara, Y. *et al.*, 1985, *supra*).

Accordingly, in a first aspect the invention features a method of treating a patient having a genetically-defined proliferative disease characterized by a non-random chromosomal aberration. This aberration produces or is capable of producing an oncogenic fusion protein. The method in its broadest embodiment includes (a) providing a



cell, tissue, or fluid sample of a patient suspected of having a genetically-defined proliferative disease; (b) identifying in the cell, tissue, or fluid sample one or more characteristics indicative of the proliferative disease; and (c) administering to the patient a pharmaceutically effective amount of an HSP90-inhibiting compound.

5 The patient may be any organism that can manifest a proliferative disease characterized by an oncogenic fusion protein, which disease is responsive to HSP90 inhibitors. Preferably, but not necessarily, the organism is an animal, more preferably a mammal, and most preferably a human.

10 In preferred embodiments, the inhibitory compound is an ansamycin including but not limited to, *e.g.*, geldanamycin, the geldanamycin derivative, 17-AAG, herbimycin A, and/or macbecin. Most preferably, the ansamycin is 17-AAG. These and other ansamycins and methods of preparing them are well-known in the art. *See, e.g.*, US Patents 3,595,955, 4,261,989, 5,387,584, and 5,932,566. Although preferably the compound is an ansamycin, the method may make use of any compound, synthetic or  
15 nonsynthetic, that can inhibit HSP90. Preferably, the inhibitor binds the ATP-binding site of HSP90, or an HSP90 homolog. Radicicol is a nonsynthetic example of a compound useful in the invention described and claimed herein. Libraries of small molecules, synthetic and/or nonsynthetic exist or can be made according to routine, well-known methods and screened for HSP90 binding and/or inhibitory activity. These molecules with  
20 HSP90 binding and/or inhibitory activity are also useful in the methods of the invention.

In the identifying step of the invention, which is carried out prior to diagnosis where/when there is no previous diagnosis, any technique can be used that can identify or predict a proliferative disorder targetable by HSP90 inhibitors. Especially preferred are antibody-based and nucleic acid hybridization and/or amplification techniques.

25 Immunoprecipitation, western blotting, and immunoblotting are illustrative examples of antibody-based methods. The antibodies may be monoclonal and/or polyclonal. Illustrative examples of nucleic acid hybridization-based techniques involve Southern blotting, northern blotting, and dot-blotting. Illustrative examples of nucleic acid amplification include standard polymerase chain reactions and variations thereof, *e.g.*,  
30 reverse transcriptase-PCR (RT-PCR). The latter is especially useful for identifying levels of gene expression. Other techniques such as the ligase chain reaction (LCR) are also

well-known and have the ability to distinguish an aberrant gene (and indirectly a protein product produced therefrom) from a normal one, or at least predict genotype and/or phenotype. Other methods of identification include ligand-binding assays and gel-retardation assays that display characteristic binding affinities and/or mobility profiles for normal and variant proteins. Where the fusion protein is also an enzyme, one can establish and/or measure aberrance by enzymatic activity (or lack thereof). Conventional and derivative karyotyping and cytochemical techniques can also be used to identify a proliferative disorder of the invention prior to administration of HSP90-inhibitors. One such method is fluorescent *in situ* hybridization (FISH).

In some embodiments, the proliferative disease is a hematopoietic disorder including but not limited to one selected from the group consisting of T or B cell lymphomas, chronic myeloid leukemias (CMLs), acute promyelocytic leukemias (APLs), acute lymphoid or lymphoblastic leukemias (ALLs), acute myeloid leukemias (AMLs), non-Hodgkin lymphomas (NHLs), and chronic myelomonocytic leukemias (CMMLs). In other embodiments, the disease is characterized by a solid tumor, preferably including but not limited to papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, synovial sarcoma. The embodiments are not necessarily mutually exclusive of one another, and treatment of multiple distinct diseases may simultaneously be effected in a given patient, as the invention has broad-spectrum merit against a variety of different proliferative disorders.

Targeted fusion proteins may contain one or more functional domains or portions thereof, e.g., kinases, DNA binding motifs, etc. Such domains are well-known in the art. Figure 1 illustrates several types of these domains, and the specific fusion proteins, genes, and diseases they can be associated with.

Administration may be by a variety of means. In some preferred embodiments, administration is made *ex vivo*, e.g., removing and treating blood or tissue that is thereafter administered back into the patient. Alternatively, or in combination, administration may be intralesional, e.g., administered to the site of a solid tumor, and/or parenteral. These constitute just some of the many different modes of administration that can be used.

Others are described herein.

In other embodiments, the HSP90-inhibiting compound has an  $IC_{50}$  that is higher (preferably two-fold, more preferably five-fold, and most preferably ten-fold) for cells that do not have characteristics indicative of the proliferative disorder as compared with those cells that do have such characteristics.

In other embodiments, the patient may be tested pre- and/or post-administration for sensitivity and/or effect of one or more HSP90 inhibitors. This may be done *in vitro* or *in vivo*.

Numerous non-random chromosomal aberrations exist that are associated with proliferative disorders. These include but are not limited to chromosomal translocations, inversions, and deletions. Duplications also account for some aberrant chromosomes and aberrant resulting gene products. All aberrations can be targeted in various aspects of the invention. Illustrative examples of specific aberrations include those listed in Figure 1, which is adapted from Table 1 of Rabbitts, Nature 372:143-149 (1994), and others including but not limited to: inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), 9; 9?, t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9; 12)(q34;p13), del(12p), t(9; 22), +8, +Phi.i(17q), t(15; 17)(q22; q12), t(11; 17)(q23; q12), t(16; 16)(p13; q22), inv(16)(p13; q22), t(9; 11)(p22; q23), t(1; 22)(p13; q13), t(3; 3)(q21; q26), inv(3)(q21q26), t(3; 5)(q21; q31), t(3; 5)(q25; q34), t(7; 11)(p15; p15), t(8; 16)(p11; p13), t(9; 12)(q34; p13), t(12; 22)(p13; q13), del(5q), del(7q), del(20q), t(11q23), t(12; 21)(p13; q22), t(5; 12)(q31; p13), t(1; 12)(q25; p13), t(12; 15)(p13; q25), t(1; 12)(q21; p13), t(12; 21)(q13; p32), and t(5; 7)(q33; q11.2). These are merely a sampling of the many chromosomal aberrations well-known in the art that give rise to particular proliferative disorders treatable according to the invention. For these and others, see, e.g., the National Center for Biotechnology Information (NCBI) databases, including, e.g., the Online Mendelian Inheritance in Man (OMIM) database and related links to nucleotide and protein sequences. For purposes of the present invention, the underlying genetic sequences affected are for the most part known and/or may be deduced using techniques routine in the art.

Targeted in particularly preferred embodiments of the invention are chromosomal aberrations corresponding to t(9; 22)(q34; q11) that give rise to bcr-abl fusion proteins, chronic myelogenous leukemia (CML) and, in some cases, acute lymphoid or lymphoblastic leukemia (for ALL, see, e.g., Erikson et al., *Heterogeneity of chromosome 22 breakpoint in Philadelphia-positive (Ph<sup>+</sup>) acute lymphocytic leukemia*, Proc. Nat. Acad. Sci. 83: 1807-1811 (1986))).

In a second aspect, the invention features a method of treating cancerous cells in a heterogeneous population of cells. The heterogeneous population includes both cancerous and noncancerous cells, and the cancerous cells are further characterized by fusion proteins that are not produced in the noncancerous cells. The method includes administering to the heterogeneous population a pharmaceutically effective amount of an HSP90-inhibiting compound. The population may be tested by separation of samples from each population into separate subpopulations, cancerous or noncancerous, e.g., where cultured cells of each are tested in parallel for response and/or susceptibility to an HSP90-inhibitor or candidate inhibitor molecule. Alternatively, the population may be mixed, e.g., in an *ex vivo* procedure in which cells of a patient, e.g., blood, are treated and administered back to the patient or to another individual. This method otherwise tracks the various described and/or claimed embodiments and/or combinations of embodiments of the first aspect.

In a third aspect, the invention features a method of treating a patient having a proliferative disease associated with a mutant protein or cellular protein isoform dependent on HSP90, or which disease is otherwise sensitive to HSP90 inhibitors. The method includes (a) providing a cell, tissue, or fluid sample of a patient suspected of having said proliferative disease; (b) identifying in the cell, tissue, or fluid sample one or more characteristics indicative of a mutant or cellular protein isoform; and (c) administering to the patient a pharmaceutically effective amount of an HSP90-inhibiting compound.

In preferred embodiments, the mutant protein or cellular protein isoform is selected from the group consisting of src, RET, p53, p51, p63, and p73. Most preferably selected are isoforms of p53 selected from N239S, C176R, and R213\*, Y236delta, C174Y, M133T, G245D, E258K, 1-293delta, G245C, R248W, E258K, R282W, R175H, R280K,

V143A, R175H, P177S, H178P, H179R, R181P, 238-9delta, G245S, G245D, M246R, R248Q, R249S, R273H, R273C, R273L, and D281Y.

In another preferred embodiment, the proliferative disease to be treated is rheumatoid arthritis.

5 In some embodiments, the mutant protein or cellular protein isoform may give rise to a dominant negative phenotype. In other embodiments, the mutant or cellular protein isoform may give rise to a dominant positive mutant. In either embodiment, the patient may be heterozygous for the normal cellular gene. Other embodiments track those listed for the preceding aspects.

10 In a fourth aspect, the invention features a method of selectively treating cells that express a mutant protein or cellular protein isoform associated with a proliferative disorder and which mutant/isoform is dependent on HSP90, or which disease is otherwise sensitive to HSP90 inhibitors. The method includes (a) providing a population of cells in which at least some of the population express a mutant protein or cellular protein isoform that is  
15 dependent on HSP90 or which are otherwise sensitive to HSP90 inhibitors. The method further includes administering to the population a pharmaceutically effective amount of an HSP90-inhibiting compound. The embodiments for this aspect may otherwise track preceding embodiments.

The foregoing aspects contemplate treatment of existing cell proliferative  
20 disorders. It is expected that the invention may also find use in prophylactic prevention of various proliferative disorders of the invention. Further, and where appropriate, each of the embodiments discussed above and different combinations thereof, including subgenus and sub-Markush groups, may cross-apply to each of the different aspects of the invention. Further, where sequence listings are provided, the invention may in some aspects  
25 contemplate subsequences of the primary sequence listings. Any subsequence within such primary listing is also contemplated for the invention, as well as all allelic variants, and mutant variants and isoforms thereof, as well as corresponding homologs from other organisms and species. Sequences contiguous with and/or in addition to the listed sequences and their above equivalents are also contemplated.

Advantages of the invention include broad-acting treatment or prophylaxis directed to a variety of different proliferative disorders. Other advantages include the efficient and rapid diagnosis and care of patients suffering from proliferative disorders, with minimal apparent adverse effects. Still other advantages, aspects, and embodiments will be  
5 apparent from the figures, the detailed description, and the claims.

### Brief Description of the Drawings

Figure 1 illustrates various genetically defined diseases characterized by non-random chromosomal aberrations that give rise to oncogenic fusion proteins. These illustrative aberrations, diseases, and fusion proteins are targeted in various embodiments  
10 of the invention. Other targeted aberrations, diseases, and fusion proteins may be found in the specification and in sources commonly known in the art, e.g., the NCBI and GenBank databases, and journal literature.

### Detailed Description of the Invention

#### *Definitions*

15 As used herein and in the claims the following terms have the following meanings:

A "genetically-defined disease" is one with a basis in DNA. Genetically defined diseases of the invention include "cell proliferative disorders" wherein unwanted cell proliferation of one or more subset(s) of cells in a multicellular organism occurs, resulting in harm, for example, pain or decreased life expectancy to the organism. "Cell proliferative disorders" refer to disorders  
20 wherein unwanted cell proliferation of one or more subset(s) of cells in a multicellular organism occurs, resulting in harm, for example, pain or decreased life expectancy to the organism. Cell proliferative disorders include, but are not limited to, cancers, tumors, benign tumors, blood vessel proliferative disorders, autoimmune disorders and fibrotic disorders. These disorders are not necessarily independent. For example, fibrotic disorders may be related to, or overlap with,  
25 blood vessel disorders, e.g., atherosclerosis (which is characterized herein as a blood vessel disorder that is associated with the abnormal formation of fibrous tissue).

A "non-random chromosomal aberration" is one that occurs with a nonrandom frequency or is selected for in a population of individuals. Chromosomal aberrations of the invention include translocations, i.e., relocation of a fragment of one chromosome onto another

chromosome; inversions, *i.e.*, wherein pieces of a chromosome rotate within the same chromosome, and deletions, *i.e.*, wherein fragments of a chromosome are lost thereby juxtaposing pieces of DNA that previously did not reside immediately beside each other.

5 An "oncogenic fusion protein" is a protein that is non-natural in and of itself but that may contain one or more pieces of other proteins that may or may not naturally occur within a cell. The fusion protein functions by improperly stimulating cell growth, directly or indirectly. In the context of the invention, the term is also associated with a cellular proliferative disease and is preferably encoded by a nucleic acid found in the cell, *e.g.*, as part of a non-random chromosomal aberration. An oncogenic fusion protein may contain domains or portions thereof, *e.g.*, kinases  
10 and/or DNA binding proteins that are well known in the art, or else predicted from their structure to behave as such.

A "fusion" may relate to, as appropriate to a given context, a fusion chromosome, an abnormal mRNA transcribed from the fused portion of the chromosome, or a polypeptide product translated from the abnormal mRNA that is transcribed from the fusion chromosome. These  
15 fusions may result from chromosomal deletions, insertions, and/or translocations. Domains or portions of different genes and gene products are frequently, although not necessarily always, brought together as a consequence of the fusion event. For example, an intragenic deletion can result in an intragenic fusion and give rise to an abnormal protein lacking a component from a second gene. More frequently it occurs that two genes or portions thereof are juxtaposed more or  
20 less, transcribed together as a single transcript, and translated together as a fusion protein bearing contributions from multiple genes or other chromosomal DNA pieces. In such fusions, reading frames can be preserved, *e.g.*, as in preserved functional domains or portions thereof coming from two or more different genes, or else the reading frame can be disrupted, *e.g.*, as in the case of a "missense" or "nonsense" event as these terms are known in the art.

25 By "providing a cell, tissue, or fluid sample of a patient suspected of having said genetically-defined disease" and "identifying one or more characteristics indicative of said disease in or on said cell, tissue, or fluid sample" can mean, although is not limited to the situation where, the sample is withdrawn from the patient in order to perform the analysis or analyses. Many invasive and noninvasive procedures exist, *e.g.*, NMR, ultrasound and other imaging techniques,  
30 that can be used to diagnose, at least in part, an illness and its cause. For example, "tagged" antibodies or other ligands with affinity for a fusion protein or chromosomal aberrancy or

aberrancy product of the invention can be used to make the diagnosis and/or assist in treatment according to methods of the invention.

“Characteristics indicative of said disease” may embrace phenotypes or genotypes and may be measured qualitatively or quantitatively by a variety of techniques. The characteristics may be observed with the naked eye or else through the assistance of a machine or other diagnostic technique(s). Exemplary techniques of measurement include but are not limited to immunoreactivity and/or precipitation, PCR, LCR, karyotyping, and fluorescence activated cell sorting (“FACS”) as those terms are known and understood in the art.

“Administering” can be by direct means, *e.g.*, intralesional or by parenteral or peripheral administration to a patient, or else by indirect means, *e.g.*, as by withdrawing a patient’s cells, treating them, and then re-introducing them back into the patient. The latter constitutes an “*ex vivo*” technique.

An “HSP90-inhibiting compound” is one that disrupts the expression, structure, and/or function of an HSP90 chaperone protein and/or a protein that is dependent on HSP90. HSP90 proteins are highly conserved in nature (see, *e.g.*, NCBI accession #'s P07900 and XM 004515 (human  $\alpha$  and  $\beta$  HSP90, respectively), P11499 (mouse), AAB2369 (rat), P46633 (chinese hamster), JC1468 (chicken), AAF69019 (flesh fly), AAC21566 (zebrafish), AAD30275 (salmon), O02075 (pig), NP 015084 (yeast), and CAC29071 (frog). There are thus many different HSP90s, all with anticipated similar effect and similar inhibition capabilities. The HSP90 inhibitor used in the methods of the invention may be specifically directed against an HSP90 of the specific host patient or may be identified based on reactivity against an HSP90 homolog from a different species, or an artificial HSP90 variant. The inhibitors used may be ring-structured antibiotics, *e.g.*, benzoquinone ansamycins, or other types of molecules, *e.g.*, antisense nucleic acids and molecules such as radicicol.

An “ansamycin” includes but is not limited to geldanamycin, 17-AAG, herbimycin A, and mabecin. The specific ansamycin 17-AAG stands for 17-allylamino-17-demethoxygeldanamycin. This and other ansamycins that can be used are well-known in the art. See, *e.g.*, U.S. Patent Nos. 3,595,955, 4, 261, 989, 5,387,584, and 5,932,566. Ansamycins may be synthetic, naturally-occurring, or else derivatives of naturally occurring ansamycins that are prepared using standard chemical derivatization techniques.



A "pharmaceutically effective amount" means an amount which is capable of providing a therapeutic or prophylactic effect. The specific dose of compound administered according to this invention to obtain therapeutic and/or prophylactic effects will, of course, be determined by the particular circumstances surrounding the case, including, for example, the specific compound administered, the route of administration, the condition being treated, the individual being treated, and the tissue or cell type targeted (or not targeted). A typical daily dose (administered in single or divided doses) will contain a dosage level of from about 0.01 mg/kg to about 100 and more preferably 50 mg/kg of body weight of an active compound of this invention. Preferred daily doses generally will be from about 0.05 mg/kg to about 20 mg/kg and ideally from about 0.1 mg/kg to about 10 mg/kg.

A preferred therapeutic effect is the inhibition to some extent of the growth of cells causing or contributing to a cell proliferative disorder. A therapeutic effect will also normally, but need not, relieve to some extent one or more of the symptoms of a cell proliferative disorder other than cell growth or size of cell mass. In reference to the treatment of a cancer, a therapeutic effect refers to one or more of the following: 1) reduction in the number of cancer cells; 2) reduction in tumor size; 3) inhibition (*i.e.*, slowing to some extent, preferably stopping) of cancer cell infiltration into peripheral organs; 3) inhibition (*i.e.*, slowing to some extent, preferably stopping) of tumor metastasis; 4) inhibition, to some extent, of tumor growth; and/or 5) relieving to some extent one or more of the symptoms associated with the disorder.

In reference to the treatment of a cell proliferative disorder other than a cancer, a therapeutic effect refers to either: 1) the inhibition, to some extent, of the growth of cells causing the disorder; 2) the inhibition, to some extent, of the production of factors (*e.g.*, growth factors) causing the disorder; and/or 3) relieving to some extent one or more of the symptoms associated with the disorder.

With respect to viral infections, the preferred therapeutic effect is the inhibition of a viral infection. More preferably, the therapeutic effect is the destruction of cells which contain the virus.

A "cancer" refers to one or more various types of benign or malignant neoplasms. In the case of the latter, these may invade surrounding tissues and may metastasize to different sites, as defined in Stedman's Medical Dictionary 25th edition (Hensyl ed. 1990).

The term "IC<sub>50</sub>" is defined as the concentration of an HSP90 inhibitor required to achieve killing or other growth inhibition of 50% of the cells of a homogenous cell type population, or of a particular cell type, *e.g.*, cancerous versus noncancerous, over a period of time. The IC<sub>50</sub> is preferably, although not necessarily, greater for normal cells than for cells exhibiting a  
5 proliferative disorder.

The term "mutant or isoform cellular protein" refers to a variation of a wild-type protein that occurs in a cell and has a particular function. The mutant or isoform cellular protein of the invention preferably associates with or gives rise to a proliferative disorder, *e.g.*, a cancer, whereas the wild-type protein ordinarily does not.

## 10 General

As described and claimed herein, ansamycins and other HSP90 inhibitors can be used to treat two important classes of tumor-promoting (oncogenic) human proteins.

### 1. Oncogenic Fusion Proteins

The first class of target proteins of the invention are fusion proteins generated as a result  
15 of non-random chromosomal aberrations (such as translocations, deletions and inversions) that juxtapose parts of the coding sequences of two normal cellular proteins (Rabbitts, T., 1994, *Nature* 372:143-149) leading to the lineage-specific expression of a mutant fusion protein that has biological activities derived from both parent proteins (Barr, F, 1998, *Nat. Genet.* 19:121-124). Without being limiting of the invention, Applicants have discovered that these fusion proteins  
20 have a heightened dependence on HSP90 chaperone activity, and/or decreased stability in the presence of HSP90 inhibitors, thus making them selective targets for treatment with HSP90 inhibitors.

#### a. Bcr-abl as an example

One example of heightened HSP90 dependence and inhibitor sensitivity is observed when  
25 chronic myelogenous leukemia (CML) cells harboring the fusion oncoprotein p210-bcr-abl are treated with HSP90 inhibitors. This fusion protein is degraded faster and more completely than wild type c-abl protein (An, W *et al.*, 2000, *Cell Growth and Differentiation* 11: 355-360). Further experimental evidence that bcr-abl expressing leukemia cells are more sensitive to HSP90 inhibitors than are closely related bcr-abl-negative leukemia lines is found in Honma, Y *et al.*,

1995, *Int. J. Cancer* 60:685-688, where it is reported that the  $IC_{50}$  of herbimycin A in six bcr-abl expressing leukemia cell lines averaged 29.3 nM as compared to a mean  $IC_{50}$  of 399.3 nM in a panel of four bcr-abl-negative leukemia lines. Illustrative protein and nucleic acid sequences corresponding to embodiments of bcr-abl fusions of the invention include but are not limited to those found in SEQ ID NOs 1-26 and subsequences thereof, which are further discussed below, along with corresponding NCBI accession numbers.

The normal Bcr gene occupies a region of about 135 kb on chromosome 22. It is expressed as mRNAs of 4.5- and 6.7-kb, which apparently encode for the same cytoplasmic 160-kD protein, and contains 23 exons as well as an unusual inverted repeat flanking the first exon. The BCR protein reportedly contains a unique serine/threonine kinase activity and at least two SH2 binding sites encoded in its first exon and a C-terminal domain that functions as a GTPase activating protein for p21(rac) (Diekmann et al., *Nature* 351: 400-402 (1991). Chisoe et al., *Genomics* 27: 67-82 (1995), sequenced the complete BCR gene and greater than 80% of the human ABL gene, which are both involved in the t(9;22) translocation (Philadelphia chromosome) associated with more than 90% of chronic myelogenous leukemia, 25 to 30% of adult and 2 to 10% of childhood acute lymphoblastic leukemia, and rare cases of acute myelogenous leukemia. Comparison of the gene with its cDNA sequence revealed the positions of 23 BCR exons and putative alternative BCR first and second exons. From the sequence of four newly studied Philadelphia chromosome translocations and a review of several other previously sequenced breakpoints, Chisoe et al. found a variety of breakpoints and recombinations sites possible within the genes. Thus, despite the normal chromosomes and genes each being known (9 and 12; bcr and abl), and the fact that combinations of these genes are known to lead to forms of CML and ALL, the precise genetic breakpoint/recombination junctions that lead to these diseases can vary.

This heterogeneity likely also applies to some non bcr-abl chromosomal aberrations of the invention as well. Nevertheless, because the genes and/or chromosomes involved are known to have a part in the disorders, the disorders are said to be "genetically defined."

## b. Other oncogenic fusion proteins

Oncogenic fusion proteins in general are thought to be inherently unstable. To the extent these unstable oncogenic fusion proteins make use of HSP90, they are susceptible of the methods claimed herein. Because the fusion genes and their protein products exert overtly oncogenic activity (Deininger, M *et al*, 2000, *Cancer Res.* 60:2049-2055), preferential degradation of these labile proteins induced by HSP90 inhibitors will have therapeutic value in diseases where the fusion protein is expressed. The present invention thus includes treatment of patients with tumors that are dependent upon other oncogenic fusion proteins that arise from non-random genetic aberrations. An illustrative but nonexhaustive list of these tumors is included in Figure 1, adapted from Table 1 of Rabbitts, T., 1994, *Nature* 372:143-149. The list may be supplemented by additional information found, *e.g.*, in Rowley, J, 1999, *Semin. Hematol.* 36:59-72 and other publications known in the art, as well as discussion below.

Myeloid cancers in particular are within the scope of the invention and include chromosomal abnormalities that give rise to oncogenic fusion proteins that drive the growth of chronic myeloid leukemia (CML), chronic myelomonocytic leukemia (CMML), acute myeloid leukemia (AML), acute promyelocytic leukemia (APL), and acute lymphoblastic leukemia (ALL). The following chromosomal aberrancies give rise to some illustrative fusions implicated in various forms of ALL:

t(1:19)(q23:p13) Pro-pre-B acute lymphoblastic leukemia

t(12:21)(p13;q32) Pro-pre-B acute lymphoblastic leukemia

t(9:22)(q34;q11) B or B-myeloid acute lymphoblastic leukemia

t(9:12)(q34:p13) Acute B-lymphoblastic leukemia

del(12p) Acute B-lymphoblastic leukemia

Specific genes and proteins thereof implicated in various ALL forms include the *MLL* gene and the *TEL* gene, which are commonly rearranged in tumors. Rowley, J, *supra*. Each has numerous fusion partners. ETV6 denotes the name of the TEL gene product. Fusion of TEL/ETV6 to an acyl CoA synthetase, ACS2, results from a t(5;12)(q31;p13) AML event (Yagasaki, F *et al*, 1999, *Genes Chromosomes Cancer* 26:192-202); fusion of TEL/ETV6 to ABL-related gene (ARG)

results from a t(1;12)(q25;p13) AML event (Iijima, Y *et al*, 2000, *Blood* 95:2126-2131); fusion of TEL/ETV6 to the neurotrophin-3 receptor TRKC results from a t(12;15)(p13;q25) AML event and gives rise to congenital fibrosarcoma (Liu, Q *et al*, 2000, *EMBO J.* 19:1827-1838, Eguchi, M *et al*, 1999, *Blood* 93:1355-1363); fusion of TEL/ETV6 to the aryl hydrocarbon receptor ARNT results from a t(1;12)(q21;p13) event and gives rise to acute myeloblastic leukemia (AML-M2) (Salomon-Nguyen, F *et al*, 2000, *Proc. Natl. Acad. Sci.* 97:6757-6762); and fusion of TEL/ETV6 to AML-1, the DNA-binding subunit of the AML-1/CBF $\beta$  transcription factor results from a (12;21)(q13;p32) event that can give rise to acute lymphoblastic leukemia (ALL, Shurtleff, SA *et al*, 1995, *Leukemia* 9:1985-1989) and, in some cases, non-Hodgkin's lymphoma (NHL).

Another illustrative fusion within the scope of the invention is the EWS/FLI-1 hybrid protein that is the hallmark of Ewing's sarcoma and the primitive neuroectodermal tumor family (Silvany, *et al*, 2000, *Oncogene* 19:4523-4530).

Yet another illustrative family of fusion proteins within the scope of the invention is the group of fusion proteins arising from chromosomal rearrangements involving the *RET* gene in thyroid cancer (Kolibaba, K, *et al*, 1997, *Biochem. Biophys. Acta* 1333:F217-F248). Rearrangements of *RET*, resulting in juxtaposition of the RET tyrosine kinase domain with one of three 5' sequences (RET-PTC-1, -2 and -3) generate fusion proteins comprising the kinase domain of RET fused to parts of the genes *H4* (RET-PTC-1), *R1a* of cAMP-dependent protein kinase A (RET-PTC-2) and *ELE-1* (RET-PTC-3).

The scope of the present invention also includes cancers and other proliferative diseases, e.g., rheumatoid arthritis, now known or discovered in the future to be characterized by specific chromosomal aberrations giving rise to fusion proteins.

In at least some cases, heterogeneity of breakpoints within the affected chromosomes is possible, thus providing for the possibility of many different DNA fusions and amino acid sequence variations than those specifically listed in the SEQ ID NOs provided, and which can also be formed by the chromosomal rearrangements, e.g., translocations, inversions, deletions, insertion/duplications, etc., so designated. For example, many different abl-bcr gene combinations and corresponding fusion proteins can be designated by the t(9;22)(q34;q11) translocation event, and all—not just those listed below—are included within the purview of the designation, t(9;22)(q34;q11).

Aberrant proteins of the invention, at least in some instances, feature one or more properties of the individual normal parent genes' gene products (normal polypeptide gene product(s), including e.g., functional and structural domains and subportions thereof resulting from transcription and translation of normal parent genes on normal  
5 chromosomes) but otherwise lack exact identity and function with the parent genes' protein products. Chromosomal aberrations may give rise to in-frame fusions or frame-shifts, the latter of which can account for missense or nonsense translation of at least a portion of the mRNA, and thereby result in aberrant polypeptide product(s).

Of the SEQ ID NOs discussed herein, some reflect fusion genes, some reflect  
10 fusion gene products, e.g., mRNAs and peptides, and some reflect portions of such entities. Still some others reflect recombination "hot spots" in the normal genes that have a general propensity to form a chromosomal aberration. Each of the above sequences may be useful as diagnostic markers in appropriate embodiments of the invention and/or may be characteristic of a given proliferative disorder (or patient exhibiting such and,  
15 accordingly, a candidate for treatment according to some methods of the invention.

While the specific sequences discussed are predominantly human in origin, it is understood that other animal "homologs" of the corresponding human sequences are known in the art and are intended to be within within the purview of various aspects of the invention. Because HSP90s are also found in plants, plants and plant cells and tissues  
20 exhibiting fusion protein products that give rise to undesirable traits may also be treatable in some aspects and embodiments of the invention. The NCBI nucleotide and protein databases are an example of where such sequences can be found. It is also appreciated that the complete human genome and other genomes have been sequenced, and continue to be sequenced at a high rate, thus facilitating the identity of sequences contiguous with  
25 those listed herein and homologs thereto.

Further, some of the sequences listed herein may contain errors associated with the logistical complexities of compiling such extensive data, and the true sequences should be interpreted to be within the scope of the invention, either literally or under the doctrine of equivalents, as they are known in the art.

30 As those of ordinary skill will appreciate, allelic variations and different isotype proteins are also possible for some genes, e.g., the product of differential splicing events in

mRNA, and these are likewise considered within the scope of the invention. Further, some of the NCBI and SEQ ID NOs listed below are for wild-type genes, and are included to give an indication of the different chimeric possibilities for the fused counterpart during a chromosomal aberration according to the invention. Should any of the sequences listed below be in error, such should be construed consistent with what is commonly understood in the art—irrespective of how presented in the application.

**c. Further Discussion of Illustrative Chromosomal Aberrancies**

*Convention: where two or more SEQ ID NOs are provided per NCBI accession #, peptide(s) shall be listed first where applicable, followed by corresponding mRNA/cDNA and/or genomic sequence as the case may be. The terms "nucleotide" and "nucleotides" are interchangeable with, and may be symbolized by, "nt."*

**t(9; 22)(q34; q11)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S72478, corresponding to SEQ ID NOs 1 and 2, illustrates one aberrant polypeptide/mRNA in a patient having CML and another patient having ALL. The junction for the nucleic acid sequence between the BCR and ABL genes is stated to reside between nucleotides 100 and 101., with 1-100 derived from BCR and 101-140 derived from ABL.

NCBI #M19695 (SEQ ID NO 3) illustrates a nucleic acid sequence identified from a human myelocytic chimeric bcr/chromosome 9 fusion (CML K562 cell line).

NCBI #M30829 (SEQ ID NOs 4 and 5) illustrates a partial bcr/abl fusion protein mRNA.

NCBI #M13096 (SEQ ID NO 6) illustrates a human chimeric bcr/c-abl fusion protein gene characteristic of cell line K562.

NCBI #M30832 (SEQ ID NOs 7 and 8) corresponds to a human bcr/abl fusion protein, partial cds, clone E3 from cell line EM2.

NCBI # AJ131466 (SEQ ID NOs 9 and 10) corresponds to a partial human bcr/abl (major breakpoint) fusion peptide and the underlying nucleic acid encoding it. Nucleotides 1-373 are said to derive from exons 11-14 of the bcr gene, and nucleotides 374-997 are said to derive from exons 2-4 of the abl gene.

NCBI # AF192533 (SEQ ID NOs 11 and 12) corresponds to a partial human bcr/abl (major breakpoint) fusion mRNA. Nucleotides 1-289 are said to come from the bcr gene of chromosome 22 and nucleotides 290-305 from the abl gene of chromosome 9.

NCBI # AF321981 (SEQ ID NO 13) corresponds to a BCR-ABL fusion transcript c15a2 mRNA sequence. This particular fusion is stated to result from results from a translocation between the 3' portion of the c-ABL oncogene on chromosome 9 and exon 15 of the BCR gene on chromosome 22; t(9;22).

NCBI # M17543 (SEQ ID NO 14) corresponds to at least a portion of a Philadelphia chromosome breakpoint cluster region associated with one embodiment of a bcr abl fusion gene. Nucleotides 1-31 are said to be exon 1 and nucleotides 32-63 are said to be intron A.

NCBI # M17542 (SEQ ID NOs 15 and 16) corresponds to a human bcr/abl fusion protein mRNA (product of translocation t(22q11; 9q34)), exons 1 and 2. Nucleotides 1-31 are stated to denote exon 1 and nucleotides 32-63 are stated to denote exon 2.

NCBI # M17541 (SEQ ID NOs 17 and 18) corresponds to a human bcr/abl fusion protein mRNA (product of translocation t(22q11; 9q34)), exons 1 and 2. Nucleotides 1-31 are stated to denote exon 1 and nucleotides 32-63 are stated to denote exon 2.

NCBI # AB069693 (SEQ ID NOs 19 and 20) denotes a human partial mRNA corresponding to a bcr/abl e8a2 fusion protein. BCR exons 7 (nucleotides 1-53) and 8 (nucleotides 54-194) are joined to ABL intron 1b inverted (nucleotides 195-249) and ABL exon a2 (nucleotides 250-423).

NCBI # AJ131467 (SEQ ID NOs 21 and 22) correspond to a human partial BCR/ABL chimeric fusion peptide and corresponding mRNA. Nucleotides 1-117 denote exon 1 of the bcr gene, nucleotides 118-193 and 194-298 denote exons 12 and 13 of the



bcr gene, and nucleotides 299-472, 473-768, and 769-922 respectively denote exons 2-4 of the abl gene.

NCBI # AF113911 (SEQ ID NOs 23 and 24) correspond to a partial BCR-ABL minor breakpoint peptide (BCR-ABL fusion) mRNA. Nucleotides 1-455 are stated to be from chromosome 22 and nucleotides 456-1079 from chromosome 9.

NCBI # AF251769 (SEQ ID NOs 25 and 26) correspond to a human partial bcr/abl e1-a3 chimeric fusion protein (BCR/ABLe1-a3) mRNA. Nucleotides 1-455 are stated to be from chromosome 22 and nucleotides 456-1079 from chromosome 9.

#### **inv14 (q11; q32)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # X82240 (SEQ ID NOs 27 and 28) correspond to at least a portion of an mRNA for the gene TCL1, which is disrupted in aberrations of the type noted.

NCBI # NM\_021966 (SEQ ID NOs 29 and 30) relate to a human T-cell leukemia/lymphoma 1A (TCL1A), mRNA.

NCBI # X82241 (SEQ ID NO 31) relates to a 5' portion of a human TCL1 gene. Nucleotides 496-560 are said to correspond to exon 1.

NCBI # M14198 (SEQ ID NOs 32 and 33) relate to a human chromosome 14 paracentric inversion producing an heavy chain/T-cell receptor J-alpha fusion protein.

NCBI # X03752 (SEQ ID NOs 34 and 35) relate to a human gene for rearranged Ig V(H) are said to encode the IgVH region (108 aa) and nucleotides 324 to 377 are said to encode 18 amino acids of the TCR-J-alpha protein.

NCBI # M12071 (SEQ ID NOs 36 and 37) relates to a human Ig heavy-chain V-region gene (VII family) rearranged to T-cell receptor alpha-chain D-J-sp region (IgT) in an inv(14)(q11; q32), SUP-T1 cell line. Nucleotides 121-166 are said to derive from exon 1 of the IgH gene, nucleotides 167-248 from intron 1 of the IgH gene, nucleotides 249-623 from exon 2 of the IgH gene, and nucleotides 624-675 from intron 2 of the IgH gene.

NCBI # S45947 (SEQ ID NOs 38 and 39) relate to an IgT=T cell specific exon ET-immunoglobulin VH-T cell receptor J alpha fusion [human, T cell lymphoma cell line SUP-T1, mRNA Mutant, 508 nt]. Nucleotides 34-507 are stated to be IgT coding sequence.

NCBI # S45207 (SEQ ID NOs 40 and 41) relate to an IgT=T cell specific exon ET-exon EX-immunoglobulin VH-T cell receptor J alpha fusion [human, T cell lymphoma cell line SUP-T1, mRNA Mutant, 616 nt]. Nucleotides 130-616 are stated to be IgT coding sequence.

**t(1; 19)(q23; p13.3)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # M31522 (SEQ ID NOs 42 and 43) relate to a human translocation (t1;19) fusion protein (E2A/PRL) mRNA, 3' end. ]. Nucleotides 1-1653 are stated to encode a portion of an E2A/PRL fusion protein.

**t(17; 19)(q22; p13)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # M95586 (SEQ ID NOs 44 and 45) relate to a human E2A/HLA fusion protein (E2A/HLF) mRNA, complete cds. Nucleotides 31-1755 are said to be coding sequence.

**t(15; 17)(q21-q11-22)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S50916 (SEQ ID NOs 46 and 47) relate to a PML-RAR fusion gene {fusion transcript} [human, mRNA Partial, 1284 nt]. . Nucleotides 1-1251 are said to be coding sequence.

NCBI # M73779 (SEQ ID NOs 48 and 49) relate to a human PML-RAR protein (PML-RAR) mRNA, complete cds; coding sequence: nucleotides 67-2460.

NCBI # AJ417079 (SEQ ID NOs 50 and 51) relate to a human partial mRNA for PML/RARA fusion protein (PML/RARA gene); Nucleotides 1-109 derive from exon 6 of PML, nucleotides 110-172 from intron 2 of RARA, and nucleotides 173-296 from exon 3 of RARA.

#### **t(11; 17)(q23; q21.1)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AAB29813 (SEQ ID NO 52) relates to a retinoic acid receptor alpha, RAR alpha(PLZF=zinc finger protein, PLZF-RAR alpha isoform A=fusion protein) {translocation} [human, acute promyelocytic leukemia patient, Peptide Mutant, 858 aa].

NCBI # AAB29814 (SEQ ID NO 53) relates to a PLZF=zinc finger protein(retinoic acid receptor alpha, RAR alpha, RAR alpha 1-PLZF isoform B=fusion protein) {translocation} [human, acute promyelocytic leukemia patient, Peptide Mutant, 277 aa].

#### **t(4; 11)(q21; q23)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # L22179 (SEQ ID NOs 54 and 55) relate to a human MLL-AF4 der(11) fusion protein mRNA, complete cds. Nucleotides 5-6940 are said to be coding sequence.

NCBI # S67825 (SEQ ID NOs 56 and 57) relate to a human ALL1-AF4 fusion protein mRNA, partial cds. Nucleotides 1-585 are said to derive from chromosome 11 and nucleotides 586-832 from chromosome 4.

NCBI # AF024541 (SEQ ID NOs 58 and 59) relate to a human MLL-AF4 fusion protein mRNA, partial cds. The codons are said to start with nucleotide 3.

NCBI # AF031404 (SEQ ID NOs 60 and 61) relate to a human MLL-AF4 fusion protein mRNA, partial cds. Nucleotides 1-305 are said to derive from chromosome 11 and nucleotides 306-741 from chromosome 4. Codons begin with nucleotide 3.

5 NCBI # L04731 (SEQ ID NO 63) relates to a human translocation T(4;11) of the human ALL-1 gene to chromosome 4.

NCBI # AF177237 (SEQ ID NOs 64 and 65) relate to human cell-line MV4-11, MLL/AF4 fusion protein (MLL/AF4) mRNA, partial cds. Nucleotides 1-62 derive from exon 6 of the MLL gene on chromosome 11, and nucleotides 63-450 from exon 5 of the AF4 gene on chromosome 4.

10 NCBI # AF177236 (SEQ ID NOs 66 and 67) relate to a human A1 MLL/AF4 fusion protein (MLL/AF4) mRNA, partial cds. Nucleotides 1-63 are stated to derive from exon 6 of the MLL gene on chromosome 11, and nucleotides 64-450 from exon 5 of the AF4 gene on chromosome 4.

15 NCBI # AF031403 (SEQ ID NO 68) relates to a human MLL/AF4 translocation breakpoint t(4;11)(q21;23). Nucleotides 1-105 are said to derive from exon 5 of MLL, nucleotides 435-508 from exon 6 of MLL, nucleotides 2195-2326 from exon 7 of MLL, nucleotides 2874-2987 from exon 8 of MLL, and nucleotides 3645-6983 from AF4.

20 NCBI # AF177238 (SEQ ID NOs 69 and 70) relate to a human A1 AF4-MLL fusion protein (AF4-MLL) mRNA, partial cds. Nucleotides 1-484 are said to derive from exon 3 of AF4 and nucleotides 485-596 from exon 7 of MLL.

NCBI # AF177239 (SEQ ID NOs 71 and 72) relate to a human cell-line MV4-11 AF4-MLL fusion protein (AF4-MLL) mRNA, partial cds. Nucleotides 1-484 are said to derive from exon 3 of AF4 and nucleotides 485-596 from exon 7 of MLL.

25 NCBI # AF397907 (SEQ ID NO 73) relates to a human AF4/MLL translocation breakpoint region. Nucleotides 1-437 are said to derive from intron 3 of AF6, nucleotides 440-631 from intron 6 of MLL, and nucleotides 632-747 from exon 7 of MLL. The breakpoint is approximately nucleotide 438-439, which was undetermined due to GC compressions.

NCBI # AF024543 (SEQ ID NO 74) relates to a human MLL/AF4 translocation breakpoint t(4;11)(q21;q23).

**t(9; 11)(q21; q23)**

5 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S82034 (SEQ ID NO 75) relates to an MLL-AF9=fusion gene {fusion site} [human, peripheral blood, acute myeloid leukemia FAB type M1 patient UPN 427, mRNA Partial, 60 nt].

**t(11; 19)(q23; p13)**

10 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S81007 (SEQ ID NO 76) relates to an MLL/ENL=fusion gene {rearranged derivative 11 junction region} [human, leukemic lymphoblasts, T-cell acute lymphoblastic leukemia patient RUPN2, Genomic Mutant, 74 nt]. The authors indicated that the first 34  
15 nt derived from MLL intron 8 on 11q23, and nt 35-74 from the ENL-distal region on 19p13.3

NCBI # S81008 (SEQ ID NO 77) relates to an ENL {rearranged derivative 19 junction region} [human, leukemic lymphoblasts, T-cell acute lymphoblastic leukemia patient RUPN2, Genomic Mutant, 84 nt]. The authors indicated that nt 55-84 derived  
20 from MLL gene 3' region on 11q23.

**t(X; 11)(q13; q23)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # NM\_005938 (SEQ ID NOs 78 and 79) relate to a human  
25 myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, *Drosophila*); translocated to, 7 (MLLT7), mRNA. Nucleotides 183-1688 denote an MLLT7 coding

region, with nucleotides 465-719 and 480-749 corresponding to a forkhead and forkhead domain, and G and C allelic variations possible at nucleotide 1435.

NCBI # X93996 (SEQ ID NOs 80 and 81) relate to a human mRNA for AFX protein. Nucleotides 183-1688 are said to be AFX coding sequence.

5 t(1; 11)(p32; q23)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AF331760 (SEQ ID NO 82) relates to human clone UPN5379L mRNA sequence (bone marrow acute lymphoblastic FAB L2 type).

10 t(6; 11)(q27; q23)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S82519 (SEQ ID NOs 83 and 84) relate to a human MLL-AF6 fusion protein mRNA, partial cds, identified in a leukemic patient, and with the breakpoint stated  
15 to be approximately between nt 26 and 27.

NCBI # S82521 (SEQ ID NOs 85 and 86) relate to a an MLL-AF6=fusion gene {breakpoint region, clone b} [human, blood, leukemic patient 2, mRNA Partial, 69 nt]. The breakpoint here is said to reside between nt 24 and 25.

NCBI # S82517 (SEQ ID NOs 87 and 88) relate to an MLL-AF6=fusion gene  
20 {breakpoint region} [human, blood, leukemia patient 1, mRNA Partial, 69 nt]. The breakpoint here is said to reside between nt 24 and 25.

t(11; 17)(q23; q21)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

25 NCBI # S72604 (SEQ ID NOs 89 and 90) relate to an AF17...ALL-1 {reciprocal translocation} [human, acute myeloid leukemia patient, mRNA Partial Mutant, 3 genes,

228 nt]. Nucleotides 1-88 are said to derive from AF17 and nucleotides 89-228 from ALL-1.

NCBI # (SEQ ID NOs 91 and 92) relate to a human myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, *Drosophila*); translocated to, 6 (MLLT6), mRNA.

- 5 Nucleotides approximating 22-168 are said to encode a PHD zinc finger motif and nucleotides 2185-2292 (amino acids 729-764) are said to encode a leucine zipper motif, with A and G allelic variations at nt 592 possible.

t(8; 21)(q22; q22)

- This translocation is generally addressed in Figure 1. Illustrative embodiments  
10 include but are not limited to events comprising the sequences:

NCBI # (SEQ ID NOs 93 and 94) relate to a human mRNA for AML1-MTG8 fusion protein, complete cds. The coding sequence is said to be nucleotides 1579-3837 and the breakpoint is said to be between nt 2110 and 2111.

- NCBI # S78158 (SEQ ID NOs 95 and 96) relate to a human AML1-ETO fusion  
15 protein (AML1-ETO) mRNA, partial cds. Nucleotides 1-1767 are said to denote the coding sequence.

NCBI # S78159 (SEQ ID NOs 97 and 98) relate to a human AML1-ETO fusion protein (AML1-ETO) mRNA, partial cds. . Nucleotides 1-696 are said to denote the coding sequence and nucleotides 40 and 41 are said to represent the junction point.

- NCBI # D14822 (SEQ ID NOs 99 and 100) relate to a human chimeric partial  
20 mRNA derived from AML1 and MTG8(ETO) gene sequences. Nucleotides 1-101 are said to derive from the AML1 gene on chromosome 21 and nucleotides 102-799 from the MTG8 (ETO) gene on chromosome 8.

- NCBI # S45790 (SEQ ID NO 101) relates to a AML1/ETO=acute myelogenous  
25 leukemia {translocation breakpoint} [human, Genomic Mutant, 237 nt].

NCBI # Z35296 (SEQ ID NO 102) relates to a human AML1/ETO alternative fusion transcript mRNA, 276bp. Nucleotides 1-117 are said to derive from AML1 and 186-276 are said to derive from ETO.

NCBI # D14823 (SEQ ID NOs 103 and 104) relate to a human chimeric mRNA derived from AML1 gene and MTG8(ETO) gene, partial sequence. Nucleotides 1-101 are said to be derived from the AML1 gene on chromosome 21 and nucleotides 102-1446 are said to be derived from the MTG8(ETO) gene on chromosome 8, with the coding sequence denoted nt 1-757.

t(3; 21)(q26; q22)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S69002 (SEQ ID NOs 105 and 106) relate to a AML1-EVI-1=AML1-EVI-1 fusion protein {rearranged translocation} [human, leukemic cell line SKH1, mRNA Mutant, 5938 nt]. The author indicated the boundary between AML1 and EVI-1 to be between nt 2138 and 2139, with the coding sequence being 1603-5790.

NCBI # L21756 (SEQ ID NOs 107 and 108) relate to a human acute myeloid leukemia associated protein (AML1/EAP) mRNA, complete cds. Nucleotides 1-786 are said to denote the coding sequence.

NCBI # S76343 (SEQ ID NO 109) relates to AML1...EAP {translocation breakpoint} [human, chronic myelogenous leukemia in blast crisis patient, Genomic Mutant, 3 genes, 470 nt]. Nucleotides 1-125 are said to derive from AML1 and nucleotides 126-470 are said to derive from EAP.

t(16; 21)(p11; q22)

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S71718 (SEQ ID NOs 110 and 111) relate to a TLS/FUS...ERG {translocation} [human, myeloid leukemia patient, peripheral blood, bone marrow cells, mRNA Partial Mutant, 3 genes, 55 nt]. Nucleotides 46-55 are said to derive from ERG, with the codon start beginning with nt 3.

NCBI # S71805 SEQ ID NOs 112 and 113) relate to a TLS/FUS...ERG {translocation} [human, myeloid leukemia patient, peripheral blood, bone marrow cells,



mRNA Partial Mutant, 3 genes, 99 nt]. Nucleotides 1-89 are said to derive from TLS/FUS and nucleotides 90-99 from ERG, with the codon start beginning with nt 3.

NCBI # Y10001 (SEQ ID NO 114) relates to a DNA fragment containing fusion point of FUS gene and ERG gene, translocation t(16;21)(p11;q22).

5    **t(6; 9)(p23; q34)**

NCBI # X64229 (SEQ ID NOs 115 and 116) relate to a human dek mRNA. The coding sequence is said to be nt 34-1161.

**inv(9;9)**

10    This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # X63689 (SEQ ID NO 117) relates to a human translocation breakpoint in the "can" gene sequence. The translocation breakpoint is said to be 174..175.

NCBI # M93651 (SEQ ID NOs 118 and 119) relate to a human set gene, complete cds. The coding sequence is said to be 4-837.

15    **t(4; 16)(q26; p13)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

20    NCBI # Z14955 (SEQ ID NOs 120 and 121) relate to a human mRNA encoding the interleukin 2/BCM fusion protein. Nucleotides 1-321 derive from exons 1-3 of IL-2 and nucleotides 322-864 from the BCM gene.

**inv(16)(p13q22)**

This inversion is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

25    NCBI # AF251768 (SEQ ID NOs 122 and 123) relate to a human PCFBF/MYH11E chimeric fusion protein (CBFB/MYH11) mRNA, partial cds.

Nucleotides 1-41 correspond to exon 5 of CBFB and nucleotides 42-78 to exon 7 of MYH11.

NCBI # AF249898 (SEQ ID NOs 124 and 125) relate to a human PCBFbeta/MYH11A chimeric fusion protein (CBFbeta/MYH11A) mRNA, partial cds.  
 5 Nucleotides 1-41 correspond to exon 5 of CBFB and nucleotides 42-102 to exon 12 of MYH11.

NCBI # AF249897 (SEQ ID NOs 126 and 127) relate a human PCBFb-MYH11D chimeric fusion protein (CBFB/MYH11D) mRNA, partial cds. Nucleotides 1-41 correspond to exon 5 of CBFB and nucleotides 42-109 to exon 8 of MYH11.

10 NCBI # AF390860 (SEQ ID NO 128) relates to a human isolate UPN2 CBFB/MYH11 translocation breakpoint region sequence.

NCBI # AF390859 (SEQ ID NO 129) relates to a human isolate UPN1 CBFB/MYH11 translocation breakpoint region sequence.

15 NCBI # AF202996 (SEQ ID NOs 130 and 131) relate to human core binding factor beta-smooth muscle myosin heavy chain fusion protein (CBFB-MYH11) mRNA, partial cds. Nucleotides 1-46 are said to correspond to 16q22 and nucleotides 47-89 to 16p13. Nucleotide 50 is said to be a "t" in some cases.

**t(5; 12)(q33; p13)**

20 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # NM\_001987 (SEQ ID NOs 132 and 133) relate to a human ets variant gene 6 (TEL oncogene) (ETV6), mRNA. Nucleotides 25-1383 are said to correspond to coding sequence, of which nt 136-393 are said to correspond to a sterile alpha motif (SAM) pointed domain, nt 1036-1290 to an erythroblast transformation-specific (Ets)-  
 25 domain, and wherein allelic variations including "c"s and "t"s at each of nt 798, nt 1541, and nt 1598, and an "a"s and "c"s at each of nt 1822 and 1881.

NCBI # U11732 (SEQ ID NOs 134 and 135) relate to a human ets-like gene (tel) mRNA, complete cds. The coding sequence is said to be from nt 25-1383, and the translocation breakpoint said to occur after nt 487.

**t(2; 5)(2p23; q35)**

- 5 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI #14: AF032882 (SEQ ID NO 136) relates to a human anaplastic lymphoma kinase receptor (ALK) and nucleophosmin (NPM) truncated genes at a t(2;5) translocation breakpoint. Nucleotides 1-46 are said to be ALK sequence that is truncated at 3' due to  
10 translocation, and nucleotides 1370-1451 are said to be NPM sequence that is truncated at 5' due to translocation.

NCBI # S82740 (SEQ ID NO 137) relates to a NPM/ALK=fusion gene {translocation breakpoint} [human, lymphoma cells SUP-M2, Genomic, 1565 nt].

NCBI # S82725 (SEQ ID NO 138) relates to a NPM/ALK=fusion gene  
15 {translocation breakpoint} [human, lymphoma cells SU-DHL-1, Genomic, 1679 nt].

NCBI # U04946 (SEQ ID NOs 139 and 140) relate to a human nucleophosmin-anaplastic lymphoma kinase fusion protein (NPM/ALK) mRNA, complete cds. The recombination junction is said to occur at nt 353.

**t(11; 22) (q24; q12)**

- 20 This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AJ229320 (SEQ ID NO 141) relates to a human translocation t(11;22) DNA in ewings's tumor derivative 22 (isolate: EWTUM64/ MIC). Nucleotides 1-88 are said to denote EWS sequence and nucleotides 89-180 FLI-1 sequence.

25 NCBI # AJ229311 (SEQ ID NO 142) relates to a human translocation t(11;22) DNA in ewings's tumor derivative 22 (isolate: EWTUM56/ EW20). Nucleotides 1-114 are said to denote EWS sequence and nucleotides 115-180 FLI-1 sequence.

NCBI # AF177752 (SEQ NO 143) relates to a human clone Jugo Ewing's sarcoma-specific EWS-FLI1 chimera target sequence.

NCBI # AF177751 (SEQ ID NO 144) relates to a human Juyon Ewing's sarcoma-specific EWS-FLI1 chimera target sequence.

5 NCBI # AF177750 (SEQ ID NO 145) relates to a human clone Iti Ewing's sarcoma-specific EWS-FLI1 chimera target sequence.

NCBI # AF327066 SEQ ID NOs 146 and 147) relate to a human Ewings sarcoma EWS-Fli1 (type 1) oncogene mRNA, complete cds.

10 NCBI # XM\_060745 (SEQ ID NOs 148 and 149) relate to a human similar to EWS/FLI1 activated transcript 2 (H. sapiens) (LOC127935), mRNA. Nucleotides 10-225 and 13-195 are said to denote src homology 2 (SH2) domains.

NCBI # AF403479 SEQ ID NOs 150 and 151) relate to a human EWS/FLI1 activated transcript 2 protein mRNA, complete cds.

15 NCBI # AF020264 (SEQ ID NOs 152 and 153) relate to a human EWS/FLI1 activated transcript 2 homolog (EAT-2) gene, partial cds.

NCBI # AF020263 (SEQ ID NOs 154 and 155) relate to a Mus musculus EWS/FLI1 activated transcript 2 (EAT-2) mRNA, complete cds.

20 NCBI # S72620 SEQ ID NOs 156 and 157) relate to a EWS...Fli1 [human, T93-113 tumor, mRNA Partial Mutant, 3 genes, 229 nt]. Nucleotides 1-85 are said to denote partial EWS gene sequence and nt 86-229 are said to denote partial FLI-1 sequence.

NCBI # S64709 (SEQ ID NO 158) relates to EWS...Fli-1 {translocation} [human, IARC-EW11 Ewing's tumor-derived cells, mRNA Mutant, 3 genes, 100 nt]. Nucleotides 1-18 are said to denote partial EWS gene sequence and nt 19-100 are said to denote partial FLI-1 sequence.

25 NCBI # S62665 (SEQ ID NOs 159 and 160) relate to a type 4 EWS-FLI1 fusion {translocation} [human, primitive neuroectodermal tumor cell line TC-32, mRNA Partial Mutant, 60 nt]. Positions 1-31 are said to be from the 5' portion of EWS on chromosome

22 and positions 32-60 are said to be from the 3' (DNA-binding) region of FLI1 on chromosome 11.

### **inv(10)(q11.2; q21)**

This aberration is generally addressed in Figure 1. Illustrative embodiments

5 include but are not limited to events comprising the sequences:

NCBI # AF395885 (SEQ ID NO 161) relates to a human H4/RET fusion mRNA, partial sequence. tyrosine kinase domain of the ret. Nt 1-83 are said to derive from H4, nt 84-142 from an unidentified insertion sequence, and nt 143-447 from ret. The tyrosine kinase domain in the ret portion is said be constitutively active in the fusion product.

10 NCBI # NM\_005436 (SEQ ID NOs 162 and 163) relate to a human DNA segment, single copy, probe pH4 (transforming sequence, thyroid-1, (D10S170), mRNA. Nt 37-1794 are said to represent coding sequence, nt 202-996 said to encode a myosin tail, nt 610-999 an Ezrin/radixin/moesin family (ERM) region, with "a" and "c" allelic variation possible at nts 979, 1080, and 1445, and "a" and "g" possible at nt 1362, and "t" and "c"

15 possible at nts 1996 and 2642.

NCBI # S77910 (SEQ ID NO 164) relates to H4= gene frequently rearranged with the ret proto-oncogene {promoter} [human, Genomic, 447 nt]. Nt 442-447 are said to correspond to the coding sequence, "MA".

NCBI # S72869 (SEQ ID NOs 165 and 166) relate to H4(D10S170)=putative

20 cytoskeletal protein [human, thyroid, mRNA, 3011 nt]. Nt 37-1794 are said to correspond to coding sequence.

NCBI # X65617 (SEQ ID NO 167) relates to a human ret proto-oncogene DNA. Nt 1-54 are said to replace sequences from the H4 gene, nt 55-787 are said to correspond to an intron between the transmembrane and tyrosine kinase domain, and nt 788-808 said

25 to correspond to an exon coding for a tyrosine kinase domain.

### **t(12;22)(q13;q12)**

This translocation is generally addressed in Figure 1. Illustrative embodiments

include but are not limited to events comprising the sequences:

NCBI # NM\_005171 (SEQ ID NOs 168 and 169) relate to a human activating transcription factor 1 (ATF1), mRNA. Nt 157-252 are said to correspond to a pKID domain and nt 631-795 are said to correspond to a bZIP transcription factor region.

NCBI # AF047022 (SEQ ID NOs 170 and 171) relate to a human RNA binding protein-activating transcription factor-1 fusion protein (EWS-ATF1) mRNA, partial cds. Nt 1-65 are said to correspond to chromosome 22 and nt 66-353 to chromosome 12, with nt 66^67 said to represent the fusion junction between the EWS and ATF1 genes.

#### **t(12; 16(q13; p11))**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # AJ301614 (SEQ ID NO 172) relates to a human t(12;16)(q13;p11) translocation breakpoint (CHOP/FUS chimaeric genomic DNA). Nt 1-225 are said to correspond to the CHOP gene (chromosome 12) and nt 226-500 to the FUS gene (chromosome 16).

NCBI # AJ301613 (SEQ ID NO 173) relates to a human t(12;16)(q13;p11) translocation breakpoint (FUS/CHOP chimaeric genomic DNA). Nt 1-317 are said to correspond to the FUS gene (chromosome 16) and nt 318-521 to the CHOP gene (chromosome 12).

NCBI # AJ301612 (SEQ ID NOs 174 and 175) relate human partial mRNA for FUS/CHOP chimaeric fusion protein (type 9 transcript variant). Nt 1-118 are said to originate from chromosome 16 and nt 119-225 are said to originate from chromosome 12.

NCBI # AJ301611 (SEQ ID NOs 176 and 177) relate to a human partial mRNA for FUS/CHOP chimaeric fusion protein (type 8 transcript variant). Nt 1-128 are said to originate from chromosome 16 and nt 129-235 are said to originate from chromosome 12.

NCBI # NM\_004960 (SEQ ID NOs 178 and 179) relate to a human fusion protein derived from t(12;16) malignant liposarcoma (FUS), mRNA. Nt 79-1659 are said to denote the coding sequence. Allelic variation is stated to be possible at nts 225 (a/c), 369 (c/t), and 1586 (a/g). Nt 937-1173 are said to denote an RNA recognition motif

(RRM), and nt 1354-1425 are said to denote a zinc finger domain in a Ran binding proteins (zf-Ranbp).

NCBI # S75762 (SEQ ID NOs 180 and 181) relate to a FUS...CHOP [human, myxoid liposarcoma specimens, mRNA Partial Mutant, 3 genes, 652 nt]. Nucleotides 1-272 are said to derive from FUS.

NCBI # X71427 (SEQ ID NOs 182 and 183) relate to a human mRNA for FUS-CHOP protein fusion. Nucleotides 70-1458 are said to denote the fusion coding sequence.

NCBI # X71428 (SEQ ID NOs 184 and 185) relate to a human mRNA for FUS glycine rich protein. Nucleotides 73-1650 are said to denote the coding sequence.

NCBI # Y10004 (SEQ ID NO 186) relates to a human DNA fragment containing fusion point of FUS gene and CHOP gene, translocation t(12;16)(q13;p11). The sequence is said to contain 5'-FUS intron 7 sequence and intron 1 3' sequence from CHOP.

NCBI # Y10003 (SEQ ID NO 187) relates to a human DNA fragment containing fusion point of FUS gene and CHOP gene, translocation t(12;16)(q13;p11). The sequence is said to contain 5'-FUS intron 7 sequence and intron 1 3' sequence from CHOP.

NCBI # Y10002 (SEQ ID NO 188) relates to a human DNA fragment containing fusion point of FUS gene and CHOP gene, translocation t(12;16)(q13;p11). The sequence is said to contain 5'-FUS intron 7 sequence and intron 1 3' sequence from CHOP.

NCBI # S75763 (SEQ ID NOs 189 and 190) relate to a FUS...CHOP [human, myxoid liposarcoma specimens, mRNA Partial Mutant, 3 genes, 377 nt]. Nt 1-272 are said to derive from FUS and nt 273-377 from CHOP.

**t(2; 13)(q35;q14)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # U02308 (SEQ ID NOs 191 and 192) relate a human PAX-3-FKHR gene fusion mRNA, partial cds. Nt 1-2070 are said to be coding sequence.

**t(x;18)(p11.2;q11.2)**

This translocation is generally addressed in Figure 1. Illustrative embodiments include but are not limited to events comprising the sequences:

NCBI # S79894 (SEQ ID NOs 193 and 194) relate to a SYT...SSX {translocation  
breakpoint} [human, synovial sarcoma patient, tumor, mRNA Mutant, 3 genes, 165 nt].  
Nt 1-18 are said to derive from SYT and nt 22-165 from SSX.

NCBI # X86175 (SEQ ID NOs 195 and 196) relate to a human mRNA for SSX2 protein. Nt 92-658 are said to be coding sequence.

The following chromosomal aberrations are not discussed in Figure 1 and will now  
be discussed in more detail:

**t(12;21)(p13;q32)**

The TEL (ETV6)-AML1 (CBFA2) gene fusion is the most common reciprocal  
chromosomal rearrangement in childhood cancer, occurring in approximately 25% of the  
most predominant subtype of leukemia- common acute lymphoblastic leukemia. Ford et  
al., Proc. Natl. Acad. Sci. U.S.A. 95 (8), 4584-4588 (1998), reported characterization of  
the translocation event responsible for one TEL-AML1 genomic sequence in a pair of  
monozygotic twins diagnosed at ages 3 years, 6 months and 4 years, 10 months with  
common acute lymphoblastic leukemia. The twins shared an identical rearranged IgH  
allele. These data have implications for the etiology and natural history of childhood  
leukemia.

Other articles of interest on this subject include: Wiemels et al., *Protracted and  
variable latency of acute lymphoblastic leukemia after TEL-AML1 gene fusion in utero*,  
Blood. 1999 Aug 1;94(3):1057-62; Rubnitz et al., *The role of TEL fusion genes in  
pediatric leukemias*, Leukemia, 1999 Jan;13(1):6-13. Review; Romana et al., *The t(12;21)  
of acute lymphoblastic leukemia results in a tel-AML1 gene fusion*, Blood. 1995 Jun  
15;85(12):3662-70; Seeger et al., *TEL-AML1 fusion in relapsed childhood acute  
lymphoblastic leukemia*, Blood. 1999 94(1):374-6; Bayar et al., *Monozygotic twins with  
congenital acute lymphoblastic leukemia (ALL) and t(4;11)(q21;q23)*, Cancer Genet  
Cytogenet. 1996 Jul 15;89(2):177-80; Kobayashi et al., *Detection of the Der (21)t(12;21)*



*chromosome forming the TEL-AML1 fusion gene in childhood acute lymphoblastic leukemia*, Leuk Lymphoma. 1997 Dec;28(1-2):43-50; and Shurtleff et al., *TEL/AML1 fusion resulting from a cryptic t(12;21) is the most common genetic lesion in pediatric ALL and defines a subgroup of patients with an excellent prognosis*, Leukemia, 1995 (12):1985-9.

NCBI# AF044317 (SEQ ID NO 197) relates to a human TEL/AML1 fusion gene, partial sequence. This was derived from an ALL infant. Nts 1-407 are said to derive from TEL and nts 408-548 from AML-1.

NCBI # AF231770 (SEQ ID NO 198) relates to a human ETV6/AML1 translocation breakpoint region.

**t(9;12)(q34; p13)**

In human leukemia, activation of the ABL proto-oncogene locus on chromosome 9 most commonly occurs as a result of its fusion to the BCR locus on chromosome 22. Papadopoulos et al., Cancer Res. 55 (1), 34-38 (1995), reported a t(9;12) event—a chimeric ABL protein displaying an elevated tyrosine kinase activity fused to a TEL protein from chromosome 12. Like BCR, TEL is fused in-frame with ABL and produces a fusion protein with an elevated tyrosine kinase activity when assayed in an immune complex. The amino-terminal sequences of TEL encodes a helix-loop-helix motif which may mediate dimerization. 43: See also Okuda et al., Oncogene. 1996 Sep 19;13(6):1147-52.

NCBI # Z36279 (SEQ ID NO 199) relates to a human (9TX) breakpoint position DNA for the tel-abl fusion identified by Papadopoulos et al. The translocation breakpoint is said to reside between nt 567 and 568.

**del(12p)**

Revy et al., Cell 102:565-575 (2000), reported hyper IgM immunodeficiencies associated with deletions of 19 and 9 bases at cDNA positions 21 and 175 respectively of the activation-induced cytidine deaminase (AID) gene. The former results in a 6 amino acid deletions and a phe15 to ter premature nonsense codon. The latter results in a 3-amino acid deletion and leu59-to -phe substitution.

NCBI # AB040430 (SEQ ID NOs 200 and 201) relate to a human AID gene for activation-induced cytidine deaminase, complete cds.

NCBI # AB040431 (SEQ ID NO 202 and 203) relate to a human AID mRNA for activation-induced cytidine deaminase, complete cds. Nt 77-673 is said to be coding sequence.

NCBI # NM\_020661 (SEQ ID NOs 204 and 205) relate to a human activation-induced cytidine deaminase (AICDA), mRNA. Nt 77-673 is said to be coding sequence. Allelic variation (a/g) is said to occur at nt 541.

**t(15;17)(q22;q12)**

de The et al., Cell 1991 Aug 23;66(4):675-84, reported a PML-RAR alpha fusion mRNA generated by a t(15;17) translocation associated with acute promyelocytic leukemia (APL). The gene product contained a novel zinc finger motif common to several DNA-binding proteins and the mRNA encoded a predicted 106 kd chimeric protein containing most of the PML sequences fused to a large part of RAR alpha, including its DNA- and hormone-binding domains. In transient expression assays, the hybrid protein exhibited altered transactivating properties if compared with the wild-type RAR alpha progenitor. Identical PML-RAR alpha fusion points were found in several patients, suggesting that in APL the t(15;17) translocation generates an RAR mutant that could contribute to leukemogenesis through interference with promyelocytic differentiation.

NCBI # S50916 (SEQ ID NOs 206 and 207) relate to a PML-RAR fusion gene {fusion transcript} [human, mRNA Partial, 1284 nt]. Nt 1-1251 is said to be coding sequence.

NCBI # M73779 (SEQ ID NOs 208 and 209) relate to a human PML-RAR protein (PML-RAR) mRNA, complete cds. Nt 67-2460 is said to be coding sequence.

NCBI # AJ417079 (SEQ ID NOs 210 and 211) relate to a human partial mRNA for PML/RARA fusion protein (PML/RARA gene). Nt 1-109 are said to derive from exon 6 of PML and nts 110-172 and 173-296 are said to derive from intron 2 and exon 3 of RARA.

**t(11;17)(q23;q12)**

Chen et al., EMBO J., 12 (3), 1161-1167 (1993), reported a fusion between a novel Kruppel-like zinc finger gene and the retinoic acid receptor-alpha locus due to a variant t(11;17) translocation associated with acute promyelocytic leukaemia (APL). Chen et al identified mRNAs containing the coding sequences of the new gene, fused in-frame either upstream of the RAR alpha B region or downstream from the unique A1 and A2 regions of the two major RAR alpha isoforms. The new gene, which Chen et al. termed PLZF (for promyelocytic leukaemia zinc finger), encodes a potential transcription factor containing nine zinc finger motifs related to the Drosophila gap gene Kruppel and is expressed as at least two isoforms which differ in the sequences encoding the N-terminal region of the protein. Within the haematopoietic system the PLZF mRNAs are detected in the bone marrow, early myeloid cell lines and peripheral blood mononuclear cells, but not in lymphoid cell lines or tissues. In addition, the PLZF mRNA levels were down-regulated in NB-4 and HL-60 promyelocytic cell lines in response to retinoic acid-induced granulocytic differentiation and were very low in mature granulocytes, suggesting an important role for PLZF as well as retinoic acid and its receptors in myeloid maturation.

NCBI # NM\_006006 (SEQ ID NOs 212 and 213) relate to a human zinc finger protein 145 (Kruppel-like, expressed in promyelocytic leukemia) (ZNF145), mRNA. Nt 76-2097 are said to be coding sequence.

NCBI # Z19002 (SEQ ID NOs 214 and 215) relate to a human PLZF gene encoding kruppel-like zinc finger protein. Nt 76-2097 are said to be coding sequence.

**t(16;16)(p13;q22) and inv(16)**

Springall et al., Leukemia 12 (12), 2034-2035 (1998), identified a novel CBFβ-MYH11 fusion transcript in a patient with AML and attributed it to an inversion/translocation of chromosome 16. *See also*, Krauter et al., Genes Chromosomes Cancer. 2001 Apr;30(4):342-8, *Detection and quantification of CBFβ/MYH11 fusion transcripts in patients with inv(16)-positive acute myeloblastic leukemia by real-time RT-PCR*; Martinelli et al., Haematologica. 2000 May;85(5):552-5, *Long-term disease-free acute myeloblastic leukemia with inv(16) is associated with PCR undetectable CBFβ/MYH11 transcript*; and Dierlamm et al., Genes Chromosomes Cancer. 1998

Jun;22(2):87-94. Review, *FISH identifies inv(16)(p13q22) masked by translocations in three cases of acute myeloid leukemia.*

NCBI # AF202996 (SEQ ID NOs 216 and 217) relate to a human core binding factor beta-smooth muscle myosin heavy chain fusion protein (CBFB-MYH11) mRNA, partial cds. Nt 1-46 are said to originate from 16q22 and nt 47-89 are said to originate from 16p13. Nt 50 is said to be a "t" in some reports.

NCBI # AF251768 (SEQ ID NOs 218 and 219) relate to human PCFBF/MYH11E chimeric fusion protein (CBFB/MYH11) mRNA, partial cds. Nt 1-42 are said to derive from exon 5 of CBFB and nts 42-78 from exon 7 of MYH11.

NCBI # AF249898 (SEQ ID NOs 220 and 221) relate to a human PCFBeta/MYH11A chimeric fusion protein (CBFBeta/MYH11A) mRNA, partial cds. Nt 1-42 are said to derive from exon 5 of CBFB and nts 42-78 from exon 12 of MYH11.

NCBI # AF249897 (SEQ ID NOs 222 and 223) relate to a human s PCFBF-MYH11d chimeric fusion protein (CBFB/MYH11D) mRNA, partial cds.

NCBI # AF390860 (SEQ ID NO 224) relates to a human UPN2 CBFB/MYH11 translocation breakpoint region sequence.

NCBI # AF390859 (SEQ ID NO 225) relates to a human isolate UPN1 CBFB/MYH11 translocation breakpoint region sequence.

t(9;11)(p22;q23)

Tkachuk et al., Cell 71: 691-700, (1992), showed that the gene involved in recurring 11q23 leukemogenic translocations codes for an unusually large protein that is a homolog of Drosophila 'trithorax' and is involved in homeotic gene regulation (MLL; aka ALL1). In studies of a t(11;19) translocation, they identified a chimeric protein containing the amino-terminal 'AT-hook' motifs of the MLL gene on chromosome 11 fused to a previously undescribed protein from chromosome 19. The nucleotide sequence determinations demonstrated an open reading frame that coded for a predicted 62-kD protein, which Tkachuk et al. named ENL.

Nakamura et al., Proc. Nat. Acad. Sci. 90: 4631-4635, (1993), showed that the gene on chromosome 19 that is fused to the MLL gene in patients with leukemia and translocation t(11;19)(q23;p13) shows high sequence homology to the genes on chromosome 4 and chromosome 9 that are fused with the ALL1 gene in patients with translocation t(4;11)(q21;q23) and t(9;11)(p22;q23), respectively. The 3 protein gene products contained nuclear targeting sequences as well as serine-rich and proline-rich regions. The results suggested that the different proteins fused to ALL1 polypeptides. These leukemias provide similar functional domains.

Negrini et al., Cancer Res 1993 Oct 1;53(19):4489-92, reported potential topoisomerase II DNA-binding sites at the breakpoints of a t(9;11) chromosome translocation in acute myeloid leukemia. The event examined was a t(9;11)(p22;q23) chromosome translocation and the breakpoints on the two chromosomes occurred within introns of the involved genes: AF-9 on chromosome 9, and ALL-1 on chromosome 11. Sequence analysis identified heptamers flanking the breakpoints on both chromosomes 9 and 11, suggesting that the V-D-J recombinase was involved in the translocation. See also Cimino et al., Cancer Res. 1991 Dec 15;51(24):6712-4, *Cloning of ALL-1, the locus involved in leukemias with the t(4;11)(q21;q23), t(9;11)(p22;q23), and t(11;19)(q23;p13) chromosome translocations.*

Poirel et al., Blood 87 (6), 2496-2505 (1996), reported an MLL-AF9=fusion gene {fusion site} [human, peripheral blood, acute myeloid leukemia FAB type M1 patient UPN 427, mRNA Partial, 60 nt]; NCBI # S82034 (SEQ ID NO 226), and indicated the breakpoint to be at nucleotide 29.

t(1;22)(p13;q13)

Nakamura et al., Proc Natl Acad Sci U S A 1993 May 15;90(10):4631-5, correlated aberrations on chromosomes 4, 9, and 19 involved in 11q23 abnormalities in acute leukemia with shared sequence homology and/or common motifs, including fusions of the ENL gene with ALL-1 in (11;19) translocations. ENL proteins contain nuclear targeting sequences as well as serine-rich and proline-rich regions. Stretches abundant in basic amino acids are also present.

NCBI # AF364037 (SEQ ID NOs 227 and 228) relate to a human megakaryoblastic leukemia-1 protein/RNA-binding motif protein 15s + ae fusion protein (MKL1/RBM15 fusion) mRNA, complete cds. Ma et al., Nat. Genet. 28 (3), 220-221 (2001) identified this with an acute megakaryoblastic leukemia patient. Nt 144-221 are said to be coding sequence, with nts 1-150 deriving from chromosome 22 and nts 151-300 deriving from chromosome 1.

**t(3;3)(q21;q26) or inv(3)(q21q26)**

Ogawa et al., Oncogene 1996 Jul 4;13(1):183-91 showed that overexpression of the Evi-1 gene appears to be a consistent feature of the 3q21q26 syndrome, an association of myeloid leukemias/myelodysplastic syndrome with a specific chromosomal aberration involving both 3q21 and 3q26, such as t(3;3)(q21;q26) or inv(3)(q21q26). The rearrangement in 3q26 has been reported to occur near the Evi-1 locus, implicating that it is the critical gene deregulated in the 3q21q26 syndrome. Ogawa identified a structural abnormality of Evi-1 protein in a case with the 3q21q26 syndrome. That case carried the typical inv(3)(q21q26), in which the 3q26 breakpoint is located within an intron of the Evi-1 gene, and resulted in overexpression of a normally unexpressed, aberrant form of Evi-1 protein, in which the C-terminal 44 amino acids of wild-type Evi-1 protein were truncated and replaced by five amino acids. The truncated Evi-1 protein was shown to increase AP1 activity when expressed in NIH3T3 cells as its wild-type counterpart. The origin of this peculiar type of rearrangement of the Evi-1 gene was shown not to be an artifact during establishment of the cell line, but rather an event that occurred in the primary leukemic cells, and consistent with 3q21q26 syndrome.

NCBI # S82592 (SEQ ID NOs 229 and 230) relate to an Evi-1=Evi-1 protein {3' region, deletion region} [human, megakaryoblastoid cell line MOLM-1, chronic myelocytic leukemia patient, mRNA Partial Mutant, 916 nt]. Nt 1-132 are said to represent a partial coding sequence.

**t(3;5)(q25;q34)**

Yoneda-Kato et al., Oncogene 12: 265-275 (1996), showed that t(3;5)(q25.1;q34) of myelodysplastic syndrome and acute myeloid leukemia produces a novel fusion gene, NPM-MLF1, which results from an in-frame fusion between the 5-prime coding region of

the nucleophosmin gene on chromosome 5 and a gene on chromosome 3, designated MLF1 (myeloid leukemia factor-1). The translocation was identified in 3 t(3;5)-positive cases of AML. Expression of the mRNA was widespread but highest in testis, ovary, skeletal muscle, heart, kidney and colon. Antibodies to MLF1 detected a 31-kD protein in  
5 K562 and HEL erythroleukemia cell lines

NCBI # L49054 (SEQ ID NOs 231 and 232) relate to a t(3;5)(q25.1;p34) fusion gene NPM-MLF1 mRNA, complete cds. Nt 109-915 are said to be coding sequence.

NCBI # BC007045 (SEQ ID NOs 233 and 234) relate to a human myeloid leukemia factor 1, clone MGC:12449, mRNA, complete cds. Nt 107-913 are said to be  
10 coding sequence.

NCBI # L49054 (SEQ ID NOs 235 and 236) relate to a human t(3;5)(q25.1;p34) fusion gene NPM-MLF1 mRNA, complete cds. Nt 109-915 are said to be coding sequence.

#### **t(7;11)(p15;p15)**

15 Borrow et al., Nat. Genet. 1996 Feb;12(2):159-67, reported a t(7;11)(p15;p15) translocation in acute myeloid leukaemia that fused the genes for nucleoporin NUP98 and class I homeoprotein HOXA9.

NCBI # U41814 (SEQ ID NOs 237 and 238) relate to human NUP98-HOXA9 fusion protein mRNA, partial cds. Nt 46^47 are said to represent a NUP98-HOXA9 in-  
20 frame junction and nt 138^139 are said to be an alternative splice site within HOXA9

NCBI # NM\_002142 (SEQ ID NOs 239 and 240) relate to a human homeo box A9 (HOXA9), mRNA. Nts 67 and 213 are said to have allelic variation possible (c/g), and nt 397-567 and 397-576 are said to respectively represent a homeobox domain and a homeodomain (HOX region).

25 NCBI # U81511 (SEQ ID NOs 241, 242, and 243) relate to a human HOXA-9A and HOXA-9B (HOXA-9) gene, alternatively spliced, complete cds. Nts 145-502, 4327-4894, and 5893-6131 are said to be exon (coding) sequences, with introns present at 503-5892 and 4895-5892. Alternative splicing events are said to account for the overlap.

**t(8;16)(p11;p13)**

Panagopoulos et al., Genes Chromosomes Cancer. 2000 Aug;28(4):415-24, used RT-PCR analysis to identify MOZ-CBP and CBP-MOZ chimeric transcripts in acute myeloid leukemias with t(8;16)(p11;p13) translocations.

- 5 NCBI # AJ251844 (SEQ ID NOs 244 and 245) relate to human partial mRNA for MOZ/CBP chimeric transcript type II. Nt 1-188 are said to derive from chromosome 8 and nts 189-415 from chromosome 16.

- NCBI # AJ251845 (SEQ ID NOs 246 and 247) relate to a human partial mRNA for CBP/MOZ chimeric transcript. Nt 1-110 are said to derive from chromosome 16 and nts 111-229 from chromosome 8.
- 10

NCBI # AJ251843 (SEQ ID NOs 248 and 249) relate to human partial mRNA for MOZ/CBP chimeric transcript type I. Nt 1-188 are said to derive from chromosome 8 and nts 189-1128 from chromosome 16.

- NCBI # U47742 (SEQ ID NOs 250 and 251) relate to human monocytic leukaemia zinc finger protein (MOZ) mRNA, complete cds.
- 15

NCBI # U85962 (SEQ ID NOs 252 and 253) relate to a human CREB-binding protein mRNA, complete cds. Nt 814-8147 are said to contain coding sequence and nts 819-1124 are said to encode a nuclear receptor binding domain.

**t(9;12)(q34;p13)**

- 20 Papadopoulos et al., Cancer Res. 1995 Jan 1;55(1):34-8, reported activation of ABL by fusion to an ets-related gene, TEL.

NCBI # Z35761 (SEQ ID NOs 254 and 255) relate to a human TEL/ABL fusion protien. Nt 1-463 are said to contain a partial TEL sequence and nt 464-549 are said to contain ABL sequence.

- 25 NCBI # Z36279 (SEQ ID NO 256) relates to human (9TX) breakpoint position DNA. The breakpoint position is said to reside at 567..568.



NCBI # Z36278 (SEQ ID NO 257) relates to human (boucher) breakpoint position DNA. The breakpoint position is said to reside at 567..568.

**t(12;22)(p13;q13)**

- 5 Buijs et al., *Oncogene*. 1995 Apr 20;10(8):1511-9, reported that a t(12;22) (p13;q11) event resulted in a myeloproliferative disorders characterized by the fusion of the ETS-like TEL gene on 12p13 to the MN1 gene on 22q11.

NCBI # X85024 (SEQ ID NOs 258 and 259) relate to a human mRNA for TEL-MN1 fusion gene (type II). Nt 22..23 is said to be the fusion site.

- 10 NCBI # X85026 (SEQ ID NOs 260 and 261) relate to a human mRNA for a TEL-MN1 fusion gene (type I). Nt 22..23 is said to be the fusion site.

NCBI # X85027 (SEQ ID NOs 262 and 263) relate to a human mRNA for a MN1-TEL fusion gene (type II). Nt 22..23 is said to be the fusion site.

NCBI # X85025 (SEQ ID NOs 264 and 265) relate to a human mRNA for a MN1-TEL fusion gene (type I). Nt 22..23 is said to be the fusion site.

15 **del(5q)**

- Jaju et al., *Blood* 1999 Jul 15;94(2):773-80, reported a recurrent translocation, t(5;11)(q35;p15.5), associated with a del(5q) in childhood acute myeloid leukemia. Partial deletion of the long arm of chromosome 5, del(5q), is the cytogenetic hallmark of the 5q-syndrome, a distinct subtype of myelodysplastic syndrome-refractory anemia (MDS-RA).  
20 Deletions of 5q also occur in the full spectrum of other de novo and therapy-related MDS and acute myeloid leukemia (AML) types, most often in association with other chromosome abnormalities. However, the loss of genetic material from 5q is believed to be of primary importance in the pathogenesis of all del(5q) disorders.

- Lindgren et al., *Am J Hum Genet* 1992 May;50(5):988-97, reported phenotypic,  
25 cytogenetic, and molecular studies of three patients with constitutional deletions of chromosome 5 in the region of the gene for familial adenomatous polyposis, APC, affiliated with colon cancer and polyps. High-resolution banding studies indicated that some deletions spans the region 5q21-q22..

Other potential deletion aberrations at the 5q locus include but are not limited to deletions at positions 5q13.3, corresponding to the RASA1 gene encoding the GAP RAS p21 protein activator 1 (GTPase activating protein), aberrancies of which are known to associate with basal cell carcinoma; 5q21, corresponding to the PST gene encoding PST1 Polysialyltransferase; 5q21-q22, corresponding to the APC gene, aberrancies of which correlate with colorectal cancer; 5q31, corresponding to the FACL6 gene encoding ACS2 Fatty-acid-Coenzyme A ligase, a long-chain 6 (long-chain acyl-CoA synthetase 2), aberrancies of which give rise to myelodysplastic syndrome and acute myelogenous leukemia; 5q31, encoding the GRAF GTPase regulator associated with the focal adhesion kinase, aberrancies of which give rise to juvenile myelomonocytic leukemia; 5q31.1, encoding IRF1, a MAR Interferon regulatory factor-1, aberrancies of which give rise to macrocytic anemiam myelodysplastic syndrome (preleukemic), acute myelogenous leukemia, gastric cancer, and nonsmall cell lung cancer; 5q33.2-q33.3, corresponding to CSF1R, FMS Colony-stimulating factor-1 receptor, aberranceis of which have been associated with oncogene FMS (McDonough feline sarcoma), and predisposition to myeloid malignancy; 5q35, encoding NPM1 Nucleophosmin 1 (nucleolar phosphoprotein B23, numatrin), aberrancies of which are known to associate with acute promyelocytic leukemia; 5q35.3, encoding gene FLT4, VEGFR3, encoding PCL fins-related tyrosine kinase-4 (vascular endothelial growth factor receptor, aberrancies of which contribute to hereditary lymphedema.

NCBI # NM\_002387 (SEQ ID NOs 266 and 267) relate to a human gene that is found mutated in colorectal cancers(MCC) mRNA. Nt 221-2710 are said to represent coding sequence. Allelic variation is said to exist at nt 2869 (c/t).

#### **del(7q)**

Schwartz et al., Cytogenet. Cell Genet. 51: 152-153 (1991) reported deletion mapping of plasminogen activator inhibitor, type I (PLANHI) and beta-glucuronidase (GUSB) in 7q21-q22. Wedemeyer et al., Genomics 46: 313-315 (1997) reported the proximity of the human HIP1 gene close to the elastin (ELN) locus on 7q11.23. Dridi et al., Am. J. Med. Genet. 87: 134-138 (1999), reported skin elastic fibers in Williams syndrome and Dutly et al., Am. J. Med. Genet. 87: 134-138 (1999), reported unequal interchromosomal rearrangements corresponding to deletions in these genes, and affiliated

with Williams-Beuren syndrome. Naritomi et al., Hum. Genet. 80: 201-202 (1988), reported a microdeletion of the proximal long arm of chromosome 7 affiliated with Zellweger syndrome. Horiike et al., Leukemia. (1999) Aug;13(8):1235-42, reported distinct genetic involvement of the TP53 gene in therapy-related leukemia and myelodysplasia, with chromosomal 7 losses and their possible relationship to replication error phenotype and the development of therapy-related AML/MDS. Wong et al., Cancer Genet Cytogenet. 1995 Jul 1;82(1):70-2, reported biclonal acute monoblastic leukemia associated with del(7q). Particular sites of interest include 7q11.23, encoding PTPN12, PTPG1 Protein tyrosine phosphatase, nonreceptor-type, known to associate with colon cancer; 7q21-q22, encoding PEX1, ZWS1 Peroxisome biogenesis factor-1, associate with Zellweger syndrome-1, neonatal adrenoleukodystrophy and infantile Refsum disease; 7q22-q31.1, encoding SLC26A3, DRA, CLD Solute carrier family 26 (sulfate transporter), member 3, associated with colon cancer; 7q31-q32 SMOH, SMO Smoothened, Drosophila, homolog of 601500, associated with sporadic basal cell carcinoma.

#### **del(20q)**

A deletion in the long arm of chromosome 20 is a recurring abnormality in malignant myeloid disorders. Its occurrence suggests that the loss of genetic material on 20q provides a proliferative advantage to myeloid cells, possibly through the loss of a tumor-suppressor gene. Roulston et al., Blood 82: 3424-3429 (1993), examined a series of patients with the del(20q) using fluorescence in situ hybridization with unique sequence probes that map along the length of 20q and delineated a segment that is deleted in 95% of all patients they examined (18 of 19). In addition, they showed that the deletions are interstitial rather than terminal. The region of deletion extended from 20q11.2 to 20q12 and was flanked by RPN2 (180490) proximally and D20S17 distally. The SRC (190090) and ADA (102700) genes were found to be located within the commonly deleted segment.

Stoffel et al. (1996) generated a YAC contig map of 20q11.2-q13.1 in a region spanning about 18 Mb and representing about 40% of the physical length of 20q. The map contains the chromosomal regions deleted in MODY1 (125850) and in myeloid leukemia. Using this physical map, they refined the location of a myeloid tumor suppressor-related gene to an 18-cM interval (approximately 13 Mb) between RPN2 and D20S17.

Stoffel et al., Proc. Nat. Acad. Sci. 93: 3937-3941 (1996), correlated the occurrence of del(20q) in a broad spectrum of myeloid disorders, suggesting that the loss of genetic material on 20q could provide a proliferative advantage to myeloid cells, possibly through the loss of a tumor-suppressor gene. Stoffel et al. examined a series of patients with the del(20q) using fluorescence in situ hybridization (FISH) with unique sequence probes that map along the length of 20q, delineated a segment that is deleted in 95% of all patients examined (18 of 19), and showed that the deletions are interstitial rather than terminal. This region of deletion extends from 20q11.2 to q12, and is flanked by the RPN2 (proximal) and D20S17 loci (distal). The SRC and ADA genes are located within the commonly deleted segment.

#### t(11q23)

Shiah et al., Leukemia, (2002) 16(2):196-202, reported clinical and biological implications of partial tandem duplication of the MLL gene in acute myeloid leukemia without chromosomal abnormalities at 11q23. The clinical and biological features of acute myeloid leukemia (AML) with 11q23/MLL translocations are well known, but the characteristics of AML with partial tandem duplication of the MLL gene have not been explored comprehensively. Sheah et al analyzed MLL duplication in 81 AML patients without chromosomal abnormalities at 11q23, using Southern blotting, genomic DNA polymerase chain reaction (PCR), reverse-transcription PCR and complementary DNA sequencing. Nine patients showed partial tandem duplication of the MLL gene, including eight (12%) of the 68 with normal karyotype. Seven patients showed fusion of exon 6/exon 2 (e6/e2), one, combination of differentially spliced transcripts e7/e2 and e6/e2, and the remaining one, combination of e8/e2 and e7/e2. Among the patients with normal karyotype, children aged 1 to 15 showed a trend to higher frequency of MLL duplication than other patients (2/5 or 40% vs 6/62 or 10%,  $P = 0.102$ ). The patients with tandem duplication of the MLL gene had a significantly higher incidence of CD11b expression on leukemic cells than did those without in the subgroup of patients with normal karyotype (75% vs 28%,  $P = 0.017$ ). There were no significant differences in the expression of lymphoid antigens or other myeloid antigens between the two groups of patients. In adults, the patients with MLL duplication had a shorter median survival time than those without (4.5 months vs 12 months,  $P = 0.036$ ). In conclusion, partial tandem duplication of the MLL gene is associated with increased expression of CD11b on leukemic blasts and

implicates poor prognosis in adult AML patients. The higher frequency of MLL duplication in children older than 1 year, than in other age groups, needs to be confirmed by further studies.

Ono et al., Cancer Res. 2002 Jan 15;62(2):333-7, reported that SEPTIN6, a human  
homologue to mouse Septin6, is fused to MLL in infant acute myeloid leukemia with  
complex chromosomal abnormalities involving 11q23 and Xq24.

Borkhardt et al., Genes Chromosomes Cancer. 2001 Sep;32(1):82-8, reported an  
ins(X;11)(q24;q23) that fuses the MLL and the Septin 6/KIAA0128 gene in an infant with  
AML-M2.

Luo et al., Mol Cell Biol. 2001 Aug;21(16):5678-87, reported that ELL-associated  
factor 1 interaction domain is essential for MLL-ELL-induced leukemogenesis.

Kurwada et al., Cancer Res. 2001 Mar 15;61(6):2665-9, reported a  
t(11;14)(q23;q24) that generates an MLL-human gephyrin fusion gene along with a de  
facto truncated MLL in acute monoblastic leukemia.

Garcia-Cuellar et al., Oncogene. 2000 Mar 30;19(14):1744-51, reported that ENL,  
the MLL fusion partner in t(11;19), binds to the c-Abl interactor protein 1 (ABI1) that is  
fused to MLL in t(10;11)+.

Akao et al., Genes Chromosomes Cancer. 2000 Apr;27(4):412-7, reported an  
analysis of the rearranged genome and chimeric mRNAs caused by a t(6;11)(q27;q23)  
chromosome translocation involving MLL in an infant acute monocytic leukemia.

Hayashi et al., Cancer Res. 2000 Feb 15;60(4):1139-45, reported a leukemic cell  
line, SN-1, associated with a t(11;16)(q23;p13).

So et al., Cancer Genet Cytogenet. 2000 Feb;117(1):24-7, analysed MLL-derived  
transcripts in an infant acute monocytic leukemia having a complex translocation  
(1;11;4)(q21;q23;p16).

Kourlas et al., Proc Natl Acad Sci U S A. 2000 Feb 29;97(5):2145-50, identified a  
gene at 11q23 encoding a guanine nucleotide exchange factor that fuses with MLL in  
acute myeloid leukemia.

Taki et al., Proc Natl Acad Sci U S A. 1999 Dec 7;96(25):14535-40, reported that AF5q31, an AF4-related gene, is fused to MLL in infant acute lymphoblastic leukemia with an ins(5;11)(q31;q13q23).

Taki et al., Cancer Res. 1999 Sep 1;59(17):4261-5, reported that AF17q25, a putative septin family gene, fuses with the MLL gene in acute myeloid leukemia associated with a t(11;17)(q23;q25).

Busson-Le Coniat et al., Leukemia. 1999 Feb;13(2):302-6, reported MLL-AF1q fusion resulting from t(1;11) in an acute leukemia.

Slany et al., Mol Cell Biol. 1998 Jan;18(1):122-9, reported on the oncogenic capacity of HRX-ENL that requires the transcriptional transactivation activity of ENL and the DNA binding motifs of HRX.

Other articles of interest include, Super et al., Genes Chromosomes Cancer. 1997 Oct;20(2):185-95, *Identification of complex genomic breakpoint junctions in the t(9;11) MLL-AF9 fusion gene in acute leukemia*; Taki et al., Blood. 1997 Jun 1;89(11):3945-50, *The t(11;16)(q23;p13) translocation in myelodysplastic syndrome fuses the MLL gene to the CBP gene*; Taki Tet al., *Fusion of the MLL gene with two different genes, AF-6 and AF-5alpha, by a complex translocation involving chromosomes 5, 6, 8 and 11 in infant leukemia*; Oncogene. 1996 Nov 21;13(10):2121-30. Tanabe et al., *AF10 is split by MLL and HEAB, a human homolog to a putative Caenorhabditis elegans ATP/GTP-binding protein in an inv(10;11)(p12;q23q12)*, Blood. 1996 Nov 1;88(9):3535-45; Ma et al., *LAF-4 encodes a lymphoid nuclear protein with transactivation potential that is homologous to AF-4, the gene fused to MLL in t(4;11) leukemias*, Blood. 1996 Jan 15;87(2):734-45; Prasad et al., *Domains with transcriptional regulatory activity within the ALL1 and AF4 proteins involved in acute leukemia*, Proc Natl Acad Sci U S A. 1995 Dec 19;92(26):12160-4. Baffa et al., *Involvement of the ALL-1 gene in a solid tumor*, Proc Natl Acad Sci U S A. 1995 May 23;92(11):4922; Mitani, *Cloning of several species of MLL/MEN chimeric cDNAs in myeloid leukemia with t(11;19)(q23;p13.1) translocation*, Blood. 1995 Apr 15;85(8):2017-24; Tse et al., *A novel gene, AFIq, fused to MLL in t(1;11) (q21;q23), is specifically expressed in leukemic and immature hematopoietic cells*, Blood. 1995 Feb 1;85(3):650-6; Chen et al., *Acute promyelocytic leukemia: from clinic to molecular biology*, Stem Cells. 1995 Jan;13(1):22-31. Review; Rubnitz et al., *ENL, the*

*gene fused with HRX in t(11;19) leukemias, encodes a nuclear protein with transcriptional activation potential in lymphoid and myeloid cells, Blood. 1994 Sep 15;84(6):1747-52;*  
 Prasad et al., *Leucine-zipper dimerization motif encoded by the AF17 gene fused to ALL-1 (MLL) in acute leukemia, Proc Natl Acad Sci U S A. 1994 Aug 16;91(17):8107-11;*  
 5 Meerabux et al., *Molecular cloning of a novel 11q23 breakpoint associated with non-Hodgkin's lymphoma, Oncogene. 1994 Mar;9(3):893-8;* Gauwerky et al., *Chromosomal translocations in leukaemia, Semin Cancer Biol. 1993 Dec;4(6):333-40. Review;* Hunger et al., *HRX involvement in de novo and secondary leukemias with diverse chromosome 11q23 abnormalities, Blood. 1993 Jun 15;81(12):3197-203;* Morrissey et al., *A*  
 10 *serine/proline-rich protein is fused to HRX in t(4;11) acute leukemias, Blood. 1993 Mar 1;81(5):1124-31;* Tkachuk et al., *Involvement of a homolog of Drosophila trithorax by 11q23 chromosomal translocations in acute leukemias, Cell. 1992 Nov 13;71(4):691-700.*

**t(5;12)(q31;p13)**

Yagasaki et al. described a fusion of LACS to a TEL/ETV6 gene in an acute  
 15 myeloblastic leukemia case having a t(5;12) chromosomal translocation. The human mRNA fusion sequence may be found in NCBI # AF102845 (SEQ ID NO 268). Nt 1-40 are said to derive from the TEL gene on chromosome 12 and nt 41-1172 are said to derive from the LACS gene on chromosome 5.

**t(1;12)(q25;p13)**

Cazzaniga et al., Blood 94: 4370-4373 (1999), reported an instance of the tyrosine  
 20 kinase Abl-related gene ARG fused to ETV6 in an AML-M4Eo patient having a t(1;12)(q25;p13) translocation, and cloned reciprocal chimeric transcripts associated with the event. The ETV6/TEL gene is rearranged in most patients with 12p13 translocations fused to a number of different partners. One of the chimeric proteins consisted of the  
 25 helix-loop-helix oligomerization domain of ETV6 and the SH2, SH3, and protein tyrosine kinase domains of ABL2. The reciprocal transcript ABL2-ETV6 was also detected in the patient's RNA by RT-PCR, although at a lower expression level.

**t(12;15)(p13;q25)**

Wai et al., *Oncogene*. 2000 Feb 17;19(7):906-15, reported an ETV6-NTRK3 gene fusion associated with such translocation.

- 5 Eguchi et al., *Blood*. 1999 Feb 15;93(4):1355-63, reported a similar fusion of ETV6 to neurotrophin-3 receptor TRKC in acute myeloid leukemia with t(12;15)(p13;q25).

Knezevich et al., *Nat Genet*. 1998 Feb;18(2):184-7; reported an ETV6-NTRK3 gene fusion in congenital fibrosarcoma.

- 10 NCBI # AF125808 (SEQ ID NOs 269 and 270) relate to a human ETS related protein-neurotrophic receptor tyrosine kinase fusion protein (ETV6-NTRK3 fusion) mRNA, partial cds. Nt 12-64 are said to derive from chromosome 12 and nt 65-980 from chromosome 15.

- 15 NCBI # AF041811 (SEQ ID NOs 271 and 272) relate to a human ETS related protein-growth factor receptor tyrosine kinase fusion proteins (ETV6-NTRK3 fusion) mRNA, partial cds. . Nt 1-336 are said to derive from chromosome 12 and nt 337-1403 from chromosome 15.

**t(1;12)(q21;p13)**

- 20 Salomon-Nguyen et al., *Proc Natl Acad Sci U S A*. (2000) 97(12):6757-62, reported a t(1;12)(q21;p13) translocation observed in a case of acute myeloblastic leukemia (AML-M2). At the protein level, the untranslocated TEL copy and, as a result of the t(1;12) translocation, a fusion protein containing the amino-terminal part of TEL and essentially all of the ARNT gene (126110), were expressed. The TEL/ETV6 gene is located at 12p13 and encodes a member of the ETS family of transcription factors. Translocated ETS leukemia (TEL) is frequently involved in chromosomal translocations
- 25 in human malignancies, usually resulting in the expression of fusion proteins between the amino-terminal part of TEL and either unrelated transcription factors or protein tyrosine kinases. ARNT (aryl hydrocarbon receptor nuclear translocator) belongs to a subfamily of the "basic region helix-loop-helix" (bHLH) protein that shares an additional region of similarity called the PAS (Per, ARNT, SIM) domain. ARNT is the central partner of



several heterodimeric transcription factors, including those containing the aryl hydrocarbon (dioxin) receptor (AhR) and the hypoxia-inducible factor 1alpha (HIF1alpha). Interference with the activity of AhR or HIF1alpha may contribute to leukemogenesis.

## 2. Mutant Protein or Cellular Protein Isoforms

The second group of target proteins are mutants or isoforms (*e.g.* splice variants) of normal cellular proteins (usually the products of tumor suppressor genes) that, due to their mutant nature, exhibit a heightened dependence on HSP90 chaperone functions or else increased sensitivity, *i.e.*, instability, due to HSP90 inhibitors. The mutant or isoform proteins either (a) have become overtly oncogenic (a “dominant-positive” (DP) effect), or (b) exert a “dominant-negative” (DN) effect on their normal counterpart, thus preventing the normal protein’s tumor suppressor activity, and resulting in a net oncogenic effect. The examples are largely illustrated with respect to human sequences, although the person of ordinary skill will appreciate that homologs in other organisms are likewise included within the purview of the invention.

### a. v-src

One such example of a mutant or isoform protein is human v-src (NCBI #s NM\_005417; SEQ ID NOs 273 and 274 ), which counterpart, c-src (NCBI # XM\_044659 (SEQ ID NOs 275 and 276), corresponds to the normal cellular gene product. As described above, proteins with a heightened dependence on HSP90 can be identified by their enhanced sensitivity to degradation induced by HSP90 inhibitors, such as the ansamycin antibiotic geldanamycin. Ansamycins and other HSP90 inhibitors were originally isolated on the basis of their ability to revert v-src transformed fibroblasts (Uehara, Y. *et al.*, 1985, *Supra*, 76: 672-675) and this reversal was correlated with the functional inactivation of the v-src protein (Uehara, Y. *et al.*, 1986, *Mol. Cell. Biol.*, 6: 2198-2206). This effect was subsequently reported to be caused by the ubiquitin/proteasome-dependent degradation of the transforming v-src protein as a result of inhibition of HSP90 function by geldanamycin (Whitesell, L., *et al.*, 1994, *supra*). Finally, a recent study compared the rate and potency of degradation of v-src and c-src proteins after treatment of Rous sarcoma virus-transformed 3T3 fibroblasts with the ansamycin geldanamycin. In this study, the oncogenic mutant v-src protein was almost 100% degraded within 6 hours (An, W *et al.*, 2000, *supra*, see Figure 2), whereas the normal cellular counterpart, c-src, was largely unaffected even after 20 hours of the same treatment (An, W *et al.*, 2000, *supra*, see Figure 4).

HSP90 inhibitors can selectively induce degradation of a wide range of mutated or otherwise aberrant proteins that cause or exacerbate a disease, and that have an apparent heightened dependence on HSP90.

**b. RET**

5 An example of a dominant proto-oncogene encoding a signaling protein that is mutated in certain human cancers giving rise to constitutively active structurally abnormal cellular proteins is the *RET* proto-oncogene (NCBI # P07949; SEQ ID NO 277) in multiple endocrine neoplasia Type 2 (MEN-2). *RET* encodes a receptor tyrosine kinase whose ligand is presently unidentified (Kolibaba, K, *et al*, 1997, *Supra*). The germline mutations found in MEN-2A patients (Cys634→  
10 Arg/Tyr, similar mutations at Cys609, 611, 618 and 620) alter the tertiary structure of the protein resulting in homodimerization and activation of the kinase domain. The commonly observed mutation in MEN-2B, Met918→Thr, alters the kinase domain structure, causing activation directly. Both of these pathways involve alterations in protein conformation, which again implicates HSP90 and underscores the broad utility of the invention.

**c. p53**

15 Another example of a mutant, oncogenic variant group of a normal cellular protein is tumor suppressor antigen p53. The wild-type protein and mRNA sequences for p53 are found in NCBI accession # M14695 (SEQ ID NOs 278 and 279). However, numerous mutations in p53 are known to occur and represent the most common molecular genetic defects found in human  
20 cancers (Harris, C *et al*, 1993, *N. Engl. J. Med.* 329:1318-1327). A mutant p53 protein was reportedly degraded in cells following treatment with geldanamycin, but wild type p53 exhibited no such, or only minimal, degradation (Blagosklonny, M *et al*, 1995, *Oncogene*, 11:933-939). Unlike the situation described above for v-src, most p53 mutations are "loss of function" effects, *i.e.*, the mutation results in the inability of the protein to perform one or more of its normal  
25 functions. Thus, in a tumor cell that has an intact p53 allele and a loss of function mutant allele, simply causing the mutant form to be degraded will not change cellular behavior. However, if the mutant protein by some mechanism inhibits the action of its coexpressed normal counterpart inside tumor cells, then degrading it will affect cellular behaviour.

This "dominant-negative" (DN) effect has been shown to occur in cells harboring certain  
30 p53 mutants, and by several different mechanisms. For example, a mutant may afford tighter

DNA binding without transactivation (Chene, P, *et al*, 1999, *Int. J. Cancer*. 82:17-22). This type of p53 mutant does not exhibit “classical” DN activity unless the mutation confers an increased affinity for DNA, because the mutant stoichiometrically competes with the wild type (WT) protein for binding to DNA. Another example is inhibition of tetramerization by incorporation of one or more mutant p53s into a complex with WT proteins (Deb, D *et al*, 1999, *Int. J. Oncol*. 15:413-422, Rollenhagen, C *et al*, 1998, *Int. J. Cancer* 78:372-376). Yet a third example concerns “prion-like” activity, in which a mutant protein forces a WT protein into a mutant conformation that then impairs its ability to bind to DNA and/or transactivate p53 target genes (Chene, P, 1998, *J. Mol. Biol.* 281:205-209)

Increased stability of mutants relative to WT proteins causes them to accumulate and override normal p53 biology. This is counterintuitive given the fact that p53 has a built-in negative feedback loop on its own transcription (via induction of the mdm-2 protein, which subsequently targets p53 for degradation). If the increased stability of a given mutant were due solely to failure to transactivate mdm-2, then accumulation of the mutant would not occur in the presence of a WT allele (Blagosklonny, M, 2000, *FASEB J.* 14:1901-1907) because this protein would initiate negative feedback mechanisms that would be expected to act on both WT and mutant p53.

On the other hand, an independent mechanism favoring mutant accumulation (*e.g.* protection by association with HSP90 (Smith, D, *et al*, 1998, *supra*; Sepehria, B, *et al*, 1996, *J. Biol. Chem.* 271:15084-15090) would permit a “recessive” mutant to become in sufficient excess of the transactivating form to result in progressive inhibition of the negative feedback pathways. In this situation, the mutant would have a net DN effect due to progressive accumulation of a stoichiometric antagonist, and selective degradation of that mutant by inhibition of HSP90 activity would be expected to restore normal p53 function. Thus, in most or all cases, a DN phenotype produced by mutant p53 is secondary to the activity of HSP90 and inhibition of HSP90 function with 17-AAG or other HSP90 ATP binding site antagonists would prevent the expression of the DN phenotype and so rescue normal p53 function.

#### **i. Dominant negative p53 mutants**

A list of exemplary p53 mutations, including examples of structurally-abnormal proteins, dominant-negative proteins, prion-like proteins, and mutants with various combinations of these properties, follows:

Chene *et al*, 1999, *Int. J. Cancer* 82:17-22; Y236delta (deletion of codon 236) resulted in a conformationally altered & dominant-negative phenotype.

Preuss *et al*, 2000, *Int. J. Cancer* 88:162-171; C174Y (Cys→Tyr) (rat) is dominant-negative, non-transactivating. The same mutation at position 176 is predicted to have a similar effect in humans, as the respective homologs have close correlative structural similarities at these positions.

Srivastava *et al*, 1993, *Oncogene* 8:2449-2456; M133T (Met→Thr), G245D (Gly→Asp), and E258K (Glu→Lys) all display conformationally altered, dominant-negative, prion-like displaying activity, in that co-incubation with WT p53 converts it into the mutated conformation.

Deb *et al*, 1999, *Int. J. Oncol.* 15:413-422; 1-293delta (deletion of codons 1-293) exhibited dominant negative DNA binding characteristics without transactivating activity.

Frebourg *et al*, 1992, *Proc. Natl. Acad. Sci.* 89:6413-6417; G245C (Gly→Cys), R248W (Arg→Trp), E258K (Glu→Lys), and R282W (Arg→Try) all independently display conformationally altered, dominant-negative activity.

Brachmann *et al*, 1996, *Proc. Natl. Acad. Sci.* 93:4091-4095; novel yeast assay used to identify dominant-negative p53 mutants that have also been found in human tumors, specifically implicating codons 132, 135, 151, 158, 176, 179, 236, 241, 242, 244, 245, 246, 248, 257, 265, 273, 277, 278, 279, 280, and 281. Of particular interest because they exhibited the greatest dominant-negative activity were mutants at codons 241, 242, 244, 245, 246, 248, 277, 278, 279, 280, and 281.

Blagosklonny *et al*, 1995, *Oncogene* 11:933-939; p53s mutated at the following codons exhibited disrupted conformations were dominant negative, and sensitive to geldanamycin: R175H (Arg→His), 194, 213, 223, 248, 274, R280K (Arg→Lys).

Aurelio *et al*, 2000, *Mol. Cell. Biol.* 20:770-778; without identifying conformational status, the following mutants were identified as dominant-negative for transactivation of apoptotic signals (Bax), but not growth arrest signals (p21<sup>WAF</sup>): V143A (Val→Ala), R175H (Arg→His), G245C (Gly→Cys), R248W (Arg→Trp), R273H (Arg→His), K305M (Lys→Met), G325V (Gly→Val).

Marutani *et al*, 1999, *Cancer Res.* 59:4765-4769; yeast-based transdominance assay used to identify dominant-negative mutations at 16 codons : R156H (Arg→His), R175H (Arg→His), P177S (Pro→Ser), H178P (His→Pro), H179R (His→Arg), R181P (Arg→Pro), 238-9delta (deletion of codons 238 & 239), G245S (Gly→Ser), G245D (Gly→Asp), M246R (Met→Arg),  
 5 R248Q (Arg→Gln), R249S (Arg→Ser), R273H (Arg→His), R273C (Arg→Cys), R273L (Arg→Leu), D281Y (Asp→Tyr).

## ii. Dominant positive p53 mutants

In addition to dominant-negative mutations, some p53 mutations actually transactivate inappropriate gene expression, contributing to oncogenesis; *i.e.* a positive tumor promoting effect.

10 See Park *et al*, 1994, *Oncogene* 9:1899-1906. This type of mutation is particularly suited to the approach embodied in the present invention because, unlike in the dominant-negative situation, the presence or absence of a normal allele of the tumor suppressor gene is irrelevant to the therapeutic utility of the HSP90 inhibitor. In other words, because the mutant p53 itself contributes to the malignant process, destruction of the mutant protein by inhibition of HSP90 is  
 15 expected to have direct therapeutic value. A good example is C176Y (Cys→Tyr), as reported by Preuss, U *et al*, 2000, *Int. J. Cancer* 88:162-171. This mutant induces rather than represses the cellular fos promoter, resulting in activation of oncogenic signaling pathways. The biology of "dominant-positive" p53 mutants is reviewed in van Oijen *et al*, 2000, *Clin. Cancer Res.* 6:2138-2145. Other examples of mutations of p53 that give rise to tumorigenic phenotypes include, but  
 20 are not limited to, Phe-132, Val-135, Ala-143, His-175, His-179, Trp-248, Ser-249, Leu-273, His-273 and Gly-281. Of particular interest, because these mutant proteins have been shown to be disrupted conformationally, are Ala-143, His-175, His-179 and Gly-281 (van Oijen, M, *et al*, 2000, *supra*). Particular subsets of the above list of tumor-promoting mutants have been shown to exert their oncogenic effects via transactivation of one or more of the growth promoting genes  
 25 *bFGF*, *IGF-I*, *EGF-R*, and *c-myc*. Alternatively or conjunctively, some gain-of-function mutants, including Ala-143, His-175, Trp-248, Ser-249, His-273, and Gly-281, contribute to tumor resistance to chemotherapeutic drugs by transactivating the *MDR* gene.

As described above, in the case of this type of mutant, in heterozygous cells, selective degradation of that mutant by inhibition of HSP90 activity will restore normal p53 function.

30 Furthermore, in cases of loss of heterozygosity (LOH), where the tumor has progressed further and the second, normal p53 allele has become mutated or lost, selective degradation of the

mutated protein by inhibition of HSP90 chaperoning will result in a therapeutic effect. In this case the p53 mutant is behaving as an oncoprotein, as in the bcr-abl and v-src examples described above.

#### **d. Other tumor suppressor variant proteins**

5 In addition to p53 itself, additional members of the p53 family of tumor suppressor proteins have also been implicated in human cancer progression. Although p53 itself is a fairly ubiquitous protein, other family members have more restricted tissue distributions. In particular tissues and tumors derived therefrom, closely related non-p53 proteins serve the same role as p53 itself. In these tumors, a truncated variant, termed deltaN,  
10 predominates over the full-length form. The truncated and/or deletent isoform is able to compete with the full length form for DNA binding, but does not itself have any transactivating activity. Thus, the deltaN form inhibits the tumor suppressor activity of the full length form, so that if the variant is degraded as a result of inhibition of HSP90 activity, an antitumor effect or drug-sensitizing effect will result. The deltaN isoform will  
15 have a heightened dependence on HSP90.

The following three examples concern the specific tumor suppressor proteins p51, p63, and p73. p51 and p63 are each produced from a common 15 exon gene, p73L/p63/p51/p40/KET, and all three proteins exhibit various isoforms, including deltaN isoforms that lack N-terminal transactivation (TA) domains and which are implicated in  
20 various carcinomas treatable according to methods of the invention. The many isotypes possible for these gene products are attributable, at least in part, to complex alternative splicing events and, in the case of p63, multiple promoters. For each, it is understood that isoforms may exist and specific isoform expression patterns may vary as between different tissue types, and as between normal versus carcinomic or neoplastic tissues.

#### **i. deltaN p51**

Osada et al. described the cloning and functional analysis of human p51, which structurally and functionally resembles p53. Nature Med. 4: 839-843 (1998). Two major splicing variant gene products have been detected in normal cells, p51A and p51B. p51A (aka TAp63gamma; NCBI #s AB016072 (SEQ ID NOs 280 and 281) is a 448-amino-acid protein with  
30 a molecular weight of 50.9 kDa; and p51B (aka TAp63alpha; AB016073 (SEQ ID NOs 282 and

283) is a 641-amino-acid protein with a molecular weight of 71.9 kDa. Other encoded isoforms have also been observed, including, e.g., those denoted in the following list: p51 delta (NCBI # AF116771 (SEQ ID NOs 284 and 285), delNdelta (NCBI # AAF43493 (SEQ ID NOs 286 and 287), delNbeta (NCBI # AAF43492 (SEQ ID NOs 288 and 289), delNalpha (NCBI # AAF43491 (SEQ ID NOs 290 and 291), delNgamma (NCBI # AAF43490; SEQ ID NOs 292 and 293), TAp63delta (NCBI # AAF43489; SEQ ID NOs 294 and 295), TAp63beta (NCBI # AAF43488 (SEQ ID NOs 296 and 297), TAp63alpha (NCBI # AAF43487 (SEQ ID NOs 298 and 299), and TAp63gamma (NCBI # AAF43486 (SEQ ID NOs 300 and 301). The TA isoforms contain a transactivation domain (encoded by exon 3') for transactivating p53; the deltaN forms do not.

The absence of the TA domain is thought to render those particular isoforms nonfunctional, thereby contributing to carcinoma etiology at least when those isoforms are expressed in abnormally high amounts. Normal expression patterns of the various isotypes is known to vary as between different tissue types. In lung cancer specimens, for example, multiple deltaN ("TA-less") forms of the p51 protein were found to be overexpressed in 34 of 44 lung cancer specimens analysed (77%). (Tani, M *et al*, 1999, *Neoplasia* 1:71-79).

## ii. deltaN p63

In certain bladder and nasopharyngeal carcinomas, various isoforms of the p53 family member p63 are expressed, and one or more of the deltaN forms, e.g., deltaN p63beta (NCBI #AF075433; SEQ ID NOs 302 and 303), deltaN p63gamma (NCBI #AF075429; SEQ ID NOs 304 and 305), and deltaN p63 alpha (NCBI #AF075431 (SEQ ID NOs 306 and 307) predominate and dominantly inhibit the transactivating activity of the full length TA-containing forms. (Park, B *et al*, 2000, *Cancer Res.* 60:3370-3374). The TA-containing isoforms are TA p63 beta (NCBI #AF075432; SEQ ID NOs 308 and 309) and TA p63 alpha (NCBI #AF075430; SEQ ID NOs 310 and 311). In nasopharyngeal carcinoma, the deltaN isoform predominance is even more pronounced (Crook, T *et al*, 2000, *Oncogene* 19:3439-3444). The p63 protein is also important in UV-B-induced skin cancer. Overexpression of the deltaN isoform of p63 in transgenic mouse epidermis was found to block apoptosis induced by WT p53 in response to UV-B irradiation (Liefer, K, *et al*, 2000, *Cancer Res.* 60:4016-4020). Mutations in the p63 gene have also been reported in epidermal carcinomas. See, e.g., Osada *et al*, 1998, *Nat. Med.* 4:839-843 and NCBI #NM003722 (SEQ ID NOs 312 and 313).

## iii. deltaN p73

The p73 protein is important in ovarian carcinoma – when compared to primary cultures of normal ovarian epithelial cells, 57% of ovarian carcinoma cell lines, 71% of invasive tumors and 92% of borderline tumor tissues were found to express elevated levels of deltaN p73 (Ng, *S et al*, 2000, *Oncogene* 19:1885-1890). Full-length p73 and isoforms thereof are displayed in NCBI # Y11416 (SEQ ID NOs 314, 315, 316, and 317), along with splice and allelic variations, including splice variations responsible for the deltaN isoform.

Applicants expect that all of the foregoing truncated p53 family members are structurally unstable, dependent on HSP90 and/or exhibit increased sensitivity to HSP90 inhibitors relative to their wild-type counterparts. Applicants further anticipate that other isomeric/aberrant forms of proteins may exhibit similar behavior(s).

The methods of the present invention may be used on mammals, preferably humans, either alone or in combination with other therapies or methods useful for treating a particular cell proliferative disorder or viral infection.

The use of the present invention is facilitated by first identifying whether the cell proliferation disorder or viral infection is accompanied by cells which contain expression of a fusion oncoprotein or a mutated cellular protein with heightened dependence on HSP90 (or a fusion protein or mutant protein that, by one skilled in the art, would be predicted to have heightened dependence on HSP90). Once such disorders are identified, patients suffering from such a disorder can be identified by analysis of their symptoms by procedures well known to medical doctors. Such patients are treated as described herein.

### 3. Representative assays for diagnosing proliferative disorders

Many different types of methods are known in the art that can be used to diagnose a proliferative disorder characterized by an aberrant protein, *e.g.*, those that involve determining protein concentrations and measuring or predicting the level of proteins within cells, tissues, and fluid samples. Indirect techniques include nucleic acid hybridization and amplification using, *e.g.*, polymerase chain reaction (PCR). These techniques are known to the person of skill and are discussed, *e.g.*, in Sambrook, Fritsch & Maniatis, *Molecular Cloning: A Laboratory Manual*, Second Edition (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., Ausubel, *et al.*, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, 1994. Because the nucleic acid sequence is



known, and because the aberrant proteins have a foundational basis in the nucleic acid sequence, the specific sequences found for aberrant proteins can also be used to generate primers and probes that span the novel junction (in the case of fusion proteins), e.g., using RT-PCR and other procedures. For non-fusion proteins, as well as fusion proteins,  
5 stringent hybridization and/or PCR can be used diagnostically.

Polyclonal or monoclonal antibodies can also be generated based on the specific sequence of the aberrant protein (in the case of fusion proteins, preferably the novel amino acid junction itself) using routine techniques. See Harlow *et al.*, *Antibodies: A Laboratory Manual*, 2nd Ed; Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1988).

10 Examples of diagnostic methods of that can be used with the invention include those reviewed in Slominski, A *et al.*, 1999, *Arch. Pathol. Lab. Med.* 123:1246-1259, O'Connor *et al.*, 1999, *Leuk. Lymphoma* 33:53-63, and Scarpa, A *et al.*, 1997, *Leuk. Lymphoma* 26 Suppl. 1:77-82. A further list of methods that is intended to be exemplary but not to limit the scope of the invention, follows.

15 O'Connor *et al.*, 1997, *Br. J. Haematol.* 99:597-604 described that the t(15;17)(q22;q21) translocation found in APL produces a PML-RAR fusion protein that can be specifically detected with the 5E10 Mab by fluorescence activated cell sorting (FACS).

20 Le *et al.*, 1998, *Eur. J. Haematol.* 60:217-225 reported that the AML-ETO fusion protein that arises in t(8;21) AML can be identified in tumor cells with ETO-specific polyclonal antibodies using western blotting. The normal ETO protein (70kD) can be distinguished from the AML-ETO fusion protein (94kD) on the basis of their differing mobilities in the gel.

Viswanatha *et al.*, 1998, *Blood* 91:1882-1890 found that the CBFB-SMMHC fusion protein present in Inv(16)(p13q32) and t(16;16)(p13;q32) AML can be specifically detected with a polyclonal antibody specific for a junctional epitope using FACS of permeabilized cells.

25 In the case of dominantly-acting mutant proteins, such as mutant RET or gain-of-function mutants of p53, the presence of the specific point mutations known to give rise to the dominant mutant may be identified by the molecular genetic techniques listed above in reference to fusion proteins. Numerous reviews of germline and acquired p53 mutations detected in human cancers have been published (*see, e.g.*, Hainuit, P, *et al.*, 2000, *Adv. Cancer Res.* 77:81-137).

In the case of dominant-negative p53 mutations, several other diagnostic criteria may be employed to identify patients susceptible of treatment with the current invention. First, molecular genetic methodologies such as Southern Blotting or PCR can be used to detect the presence of a specific point mutation known to give rise to a dominant-negative version of p53. Similarly, FISH  
5 may be employed to detect specific point mutations known to confer conformational changes and/or dominant-negative activity (Villadsen R *et al*, 2000, *Cancer Genet. Cytogenet.* 116:28-34). Other methods include allele-specific PCR (AS-PCR) and chromosome flow cytometry (Villadsen *et al*, *Supra*).

Alternatively, if the mutation in question has not previously been shown to generate a  
10 dominant-negative p53 mutant, a cell-based transdominance assay may be used to determine the phenotype (Frebourg, T *et al*, 1992, *Proc. Natl. Acad. Sci.* 89:6413-6417). In this assay, p53-null SAOS-2 cells are co-transfected with WT p53 and the test mutant. The normal p53 protein causes the cells to undergo apoptosis, from which fate they can be rescued by a p53 mutant that has a dominant negative activity. In these cases, further genetic analyses may be performed to confirm  
15 the presence of an intact non-mutant allele. In addition, antibodies have been raised that distinguish between p53 proteins with normal versus mutant conformation. These latter p53s have a heightened dependence upon HSP90, and so fall within the scope of the present invention. Specifically, PAb240, from (Oncogene Sciences, Inc.) OSI, is mutant conformation-specific. The corresponding antibody specific for WT is PAb1620, also for OSI (Chene, P, *et al*, 1999, *supra*).

In the case of cell proliferative disorders arising due to unwanted proliferation of non-cancer cells, the level of the fusion protein or mutated cellular protein is compared to that level occurring in the general population (*e.g.*, the average level occurring in the general population of people or animals excluding those people or animals suffering from a cell proliferative disorder). If the unwanted cell proliferation disorder is characterized by an abnormal level of a fusion  
25 protein than occurs in a normal population, or by the presence of a mutated cellular protein, such as p53, then the disorder is a candidate for treatment using the methods described herein. In a preferred example, the mutated protein is p53 and the proliferative disorder is rheumatoid arthritis. In a particularly preferred example, the p53 mutations may include, but are not limited to, N239S (Asn→Ser), C176R (Cys→Arg) and R213\* (Arg→stop) and the mutant forms exert  
30 apparent dominant-negative activity over the wild-type protein. (Han, Z *et al*, 1999, *Arthritis Rheum.* 42:1088-1092).

#### 4. Preparation and Administration of Pharmaceutical Compositions

Geldanamycin may be prepared according to U.S. Patent No. 3,595,955 using the subculture of *Streptomyces hygroscopicus* that is on deposit with the U.S. Department of Agriculture, Northern Utilization and Research Division, Agricultural Research, Peoria, Ill., USA, accession number NRRL 3602. It is also available from Sigma/Aldrich Chemical Co., St. Louis, Mo., USA. Numerous derivatives of this compound, including herbimycin A, mabcetin, and 17-AAG may be fashioned as specified in U.S. Patent Nos. 4, 261, 989, 5,387,584, and 5,932,566, or according to standard techniques known in the art. Other useful ansamycin derivatives appear in Applicants' co-pending and commonly owned provisional application entitled, "*Ansamycins Having Improved Pharmacological and Biological Properties*," filed February 8, 2002, Serial Number to be determined, and herein incorporated by reference in its entirety.

Those of ordinary skill in the art are familiar with formulation and administration techniques that can be employed in use of the invention, e.g., as discussed in Goodman and Gilman's *The Pharmacological Basis of Therapeutics*, current edition; Pergamon Press; and Remington's *Pharmaceutical Sciences* (current edition.) Mack Publishing Co., Easton, Pa.

The compounds utilized in the methods of the instant invention may be administered either alone or in combination with pharmaceutically acceptable carriers, excipients or diluents, in a pharmaceutical composition, according to standard pharmaceutical practice. The compounds can be administered orally or parenterally, including the intravenous, intramuscular, intraperitoneal, subcutaneous, rectal and topical routes of administration.

The pharmaceutical compositions used in the methods of the instant invention can contain the active ingredient in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, hard or soft capsules, or syrups or elixirs. Compositions intended for oral use may be prepared according to any method known to the art for the manufacture of pharmaceutical compositions and such compositions may contain one or more agents selected from the group consisting of sweetening agents, flavoring agents, coloring agents and preserving agents in order to provide pharmaceutically elegant and palatable preparations. Tablets contain the active ingredient in admixture with non-toxic pharmaceutically acceptable excipients which are suitable for the manufacture of tablets. These excipients may be, for example, inert diluents, such as calcium carbonate, sodium carbonate,

lactose, calcium phosphate or sodium phosphate; granulating and disintegrating agents, such as microcrystalline cellulose, sodium crosscarmellose, corn starch, or alginic acid; binding agents, for example starch, gelatin, polyvinyl-pyrrolidone or acacia, and lubricating agents, for example, magnesium stearate, stearic acid or talc. The tablets may be uncoated or they may be coated by known techniques to mask the unpleasant taste of the drug or delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a water soluble taste masking material such as hydroxypropylmethyl-cellulose or hydroxypropylcellulose, or a time delay material such as ethyl cellulose, cellulose acetate butyrate may be employed.

Formulations for oral use may also be presented as hard gelatin capsules wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water soluble carrier such as polyethyleneglycol or an oil medium, for example peanut oil, liquid paraffin, or olive oil.

Aqueous suspensions contain the active material in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients are suspending agents, for example sodium carboxymethylcellulose, methylcellulose, hydroxypropylmethyl-cellulose, sodium alginate, polyvinyl-pyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents may be a naturally-occurring phosphatide, for example lecithin, or condensation products of an alkylene oxide with fatty acids, for example polyoxyethylene stearate, or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethylene-oxycetanol, or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan monooleate. The aqueous suspensions may also contain one or more preservatives, for example ethyl, or n-propyl p-hydroxybenzoate, one or more coloring agents, one or more flavoring agents, and one or more sweetening agents, such as sucrose, saccharin or aspartame.

Oily suspensions may be formulated by suspending the active ingredient in a vegetable oil, for example arachis oil, olive oil, sesame oil or coconut oil, or in mineral oil such as liquid paraffin. The oily suspensions may contain a thickening agent, for example beeswax, hard paraffin or cetyl alcohol. Sweetening agents such as those set forth above, and flavoring agents

may be added to provide a palatable oral preparation. These compositions may be preserved by the addition of an anti-oxidant such as butylated hydroxyanisol or alpha-tocopherol.

Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those already mentioned above. Additional excipients, for example sweetening, flavoring and coloring agents, may also be present. These compositions may be preserved by the addition of an anti-oxidant such as ascorbic acid.

The pharmaceutical compositions used in the methods of the instant invention may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil, for example olive oil or arachis oil, or a mineral oil, for example liquid paraffin or mixtures of these. Suitable emulsifying agents may be naturally-occurring phosphatides, for example soy bean lecithin, and esters or partial esters derived from fatty acids and hexitol anhydrides, for example sorbitan monooleate, and condensation products of the said partial esters with ethylene oxide, for example polyoxyethylene sorbitan monooleate. The emulsions may also contain sweetening, flavoring agents, preservatives and antioxidants.

Syrups and elixirs may be formulated with sweetening agents, for example glycerol, propylene glycol, sorbitol or sucrose. Such formulations may also contain a demulcent, a preservative, flavoring and coloring agents and antioxidant.

The pharmaceutical compositions may be in the form of sterile injectable aqueous solutions. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution and isotonic sodium chloride solution.

The sterile injectable preparation may also be a sterile injectable oil-in-water microemulsion where the active ingredient is dissolved in the oily phase. For example, the active ingredient may be first dissolved in a mixture of soybean oil and lecithin. The oil solution then introduced into a water and glycerol mixture and processed to form a microemulsion.

The injectable solutions or microemulsions may be introduced into a patient's bloodstream by local bolus injection. Alternatively, it may be advantageous to administer the solution or microemulsion in such a way as to maintain a constant circulating concentration of the instant

compound. In order to maintain such a constant concentration, a continuous intravenous delivery device may be utilized. An example of such a device is the Deltec CADD-PLUS™ model 5400 intravenous pump.

The pharmaceutical compositions may be in the form of a sterile injectable aqueous or oleaginous suspension for intramuscular and subcutaneous administration. This suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents which have been mentioned above. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally-acceptable diluent or solvent, for example as a solution in 1,3-butane diol. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

The HSP90 inhibitors used in the methods of the present invention may also be administered in the form of a suppositories for rectal administration of the drug. These compositions can be prepared by mixing the inhibitors with a suitable non-irritating excipient which is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum to release the drug. Such materials include cocoa butter, glycerinated gelatin, hydrogenated vegetable oils, mixtures of polyethylene glycols of various molecular weights and fatty acid esters of polyethylene glycol.

For topical use, creams, ointments, jellies, solutions or suspensions, etc., containing an HSP90 inhibitor can be used. (As used herein, topical application can include mouth washes and gargles.)

The compounds used in the methods of the present invention can be administered in intranasal form via topical use of suitable intranasal vehicles and delivery devices, or via transdermal routes, using those forms of transdermal skin patches well known to those of ordinary skill in the art. To be administered in the form of a transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen.

The HSP90 inhibitors used in the instant invention may also be co-administered with other well known therapeutic agents that are selected for their particular usefulness against the

condition that is being treated. For example, the instant compounds may be useful in combination with known anti-cancer and cytotoxic agents. The instant compounds may also be useful in combination with other inhibitors of parts of the signaling pathway that links cell surface growth factor receptors to nuclear signals initiating cellular proliferation.

5 The methods of the present invention may also be useful with other agents that inhibit angiogenesis and thereby inhibit the growth and invasiveness of tumor cells, including, but not limited to VEGF receptor inhibitors, angiostatin and endostatin.

When a HSP90 inhibitor used in the methods of the present invention is administered into a human subject, the daily dosage will normally be determined by the prescribing physician with  
10 the dosage generally varying according to the age, weight, and response of the individual patient, as well as the severity of the patient's symptoms.

In one exemplary application, a suitable amount of a HSP90 inhibitor is administered to a mammal undergoing treatment for cancer. Administration occurs in an amount of each type of inhibitor of between about 0.1 mg/kg of body weight to about 60 mg/kg of body weight per day,  
15 preferably of between 0.5 mg/kg of body weight to about 40 mg/kg of body weight per day. A particular therapeutic dosage that comprises the instant composition includes from about 0.01 mg to about 1000 mg of a HSP90 inhibitor. Preferably, the dosage comprises from about 1 mg to about 1000 mg of a HSP90 inhibitor.

Examples of antineoplastic agents which can be used in combination with the methods of  
20 the present invention include, in general, alkylating agents, anti-metabolites; epidophyllotoxin; an antineoplastic enzyme; a topoisomerase inhibitor; procarbazine; mitoxantrone; platinum coordination complexes; biological response modifiers and growth inhibitors; hormonal/anti-hormonal therapeutic agents and haematopoietic growth factors.

Exemplary classes of antineoplastic agents further include the anthracycline family of  
25 drugs, the vinca drugs, the mitomycins, the bleomycins, the cytotoxic nucleosides, the epothilones, discodermolide, the pteridine family of drugs, diynes and the podophyllotoxins. Particularly useful members of those classes include, for example, carminomycin, daunorubicin, aminopterin, methotrexate, methopterin, dichloromethotrexate, mitomycin C, porfiriomycin, 5-fluorouracil, 6-mercaptopurine, gemcitabine, cytosine arabinoside, podophyllotoxin or podophyllotoxin derivatives such as etoposide, etoposide phosphate or teniposide, melphalan,  
30

vinblastine, vincristine, leurosidine, vindesine, leurosine, paclitaxel and the like. Other useful antineoplastic agents include estramustine, carboplatin, cyclophosphamide, bleomycin, gemcitabine, ifosamide, melphalan, hexamethyl melamine, thiotepe, cytarabin, idatrexate, trimetrexate, dacarbazine, L-asparaginase, camptothecin, CPT-11, topotecan, ara-C, bicalutamide, 5 flutamide, leuprolide, pyridobenzoindole derivatives, interferons and interleukins.

Preferably, the pharmaceutical preparation is in unit dosage form. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component, *e.g.*, an effective amount to achieve the desired purpose.

10 The quantity of active compound in a unit dose of preparation may be varied or adjusted from about 0.1 mg to 1000 mg, preferably from about 1 mg to 300 mg, more preferably 10 mg to 200 mg, according to the particular application.

The actual dosage employed may be varied depending upon the requirements of the patient and the severity of the condition being treated. Determination of the proper dosage for a particular situation is within the skill of the art. Generally, treatment is initiated with smaller 15 dosages which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small amounts until the optimum effect under the circumstances is reached. For convenience, the total daily dosage may be divided and administered in portions during the day if desired.

The amount and frequency of administration of the HSP90 inhibitors used in the methods 20 of the present invention and, if applicable, other chemotherapeutic agents and/or radiation therapy will be regulated according to the judgment of the attending clinician (physician) considering such factors as age, condition and size of the patient as well as severity of the disease being treated. A dosage regimen of the HSP90 inhibitors can be intravenous administration of from 1 mg to 5gm/day, more preferably 10 mg to 2000 mg/day, more preferably still 10 to 1000 mg/day, and 25 most preferably 50 to 600 mg/day, in one or more (preferably two) doses, to block tumor growth.

The chemotherapeutic agent and/or radiation therapy can be administered according to therapeutic protocols well known in the art. It will be apparent to those skilled in the art that the administration of the chemotherapeutic agent and/or radiation therapy can be varied depending on the disease being treated and the known effects of the chemotherapeutic agent and/or radiation 30 therapy on that disease. Also, in accordance with the knowledge of the skilled clinician, the



therapeutic protocols (*e.g.*, dosage amounts and times of administration) can be varied in view of the observed effects of the administered therapeutic agents (*i.e.*, antineoplastic agent or radiation) on the patient, and in view of the observed responses of the disease to the administered therapeutic agents.

Also, in general, the HSP90 inhibitor and the chemotherapeutic agent do not have to be administered in the same pharmaceutical composition, and may, because of different physical and chemical characteristics, have to be administered by different routes. For example, the HSP90 inhibitor may be administered orally to generate and maintain good blood levels, while the chemotherapeutic agent may be administered intravenously. The determination of the mode of administration and the advisability of administration, where possible, in the same pharmaceutical composition, is well within the knowledge of the skilled clinician. The initial administration can be made according to established protocols known in the art, and then, based upon the observed effects, the dosage, modes of administration and times of administration can be modified by the skilled clinician.

The particular choice of HSP90 inhibitor, and chemotherapeutic agent and/or radiation will depend upon the diagnosis of the attending physicians and their judgment of the condition of the patient and the appropriate treatment protocol.

The HSP90 inhibitor, and chemotherapeutic agent and/or radiation may be administered concurrently (*e.g.*, simultaneously, essentially simultaneously or within the same treatment protocol) or sequentially, depending upon the nature of the proliferative disease, the condition of the patient, and the actual choice of chemotherapeutic agent and/or radiation to be administered in conjunction (*i.e.*, within a single treatment protocol) with the HSP90 inhibitor.

If the HSP90 inhibitor, and the chemotherapeutic agent and/or radiation are not administered simultaneously or essentially simultaneously, then the optimum order of administration of the HSP90 inhibitor, and the chemotherapeutic agent and/or radiation, may be different for different tumors. Thus, in certain situations the HSP90 inhibitor may be administered first followed by the administration of the chemotherapeutic agent and/or radiation; and in other situations the chemotherapeutic agent and/or radiation may be administered first followed by the administration of the HSP90 inhibitor. This alternate administration may be repeated during a single treatment protocol. The determination of the order of administration, and the number of repetitions of administration of each therapeutic agent during a treatment protocol,

is well within the knowledge of the skilled physician after evaluation of the disease being treated and the condition of the patient. For example, the chemotherapeutic agent and/or radiation may be administered first, especially if it is a cytotoxic agent, and then the treatment continued with the administration of the HSP90 inhibitor followed, where determined advantageous, by the administration of the chemotherapeutic agent and/or radiation, and so on until the treatment protocol is complete.

Thus, in accordance with experience and knowledge, the practicing physician can modify each protocol for the administration of a component (therapeutic agent-*i.e.*, HSP90 inhibitor, chemotherapeutic agent or radiation) of the treatment according to the individual patient's needs, as the treatment proceeds.

The attending clinician, in judging whether treatment is effective at the dosage administered, will consider the general well-being of the patient as well as more definite signs such as relief of disease-related symptoms, inhibition of tumor growth, actual shrinkage of the tumor, or inhibition of metastasis. Size of the tumor can be measured by standard methods such as radiological studies, *e.g.*, CAT or MRI scan, and successive measurements can be used to judge whether or not growth of the tumor has been retarded or even reversed. Relief of disease-related symptoms such as pain, and improvement in overall condition can also be used to help judge effectiveness of treatment.

## EXAMPLES

The following examples are illustrative only, and are not intended to be limiting of the invention.

### Example 1:

#### Cytotoxic Activity of 17AAG on K562 Versus a Normal Cell Type

Grosveld et al., Mol Cell Biol 6(2):607-16 (1986) showed that the chronic myelocytic cell line K562 produces a chimeric bcr/c-abl transcript, making it a suitable model system to demonstrate the methods of the invention. The cell line is widely available, *e.g.*, from American Type Culture Collection ("ATCC"; Manassas, VA, USA; cat# CCL-243) and can be propagated in a variety of media, *e.g.*, ATCC's Iscove's modified Dulbecco's medium with 4 mM L-glutamine adjusted to contain 1.5 g/L sodium bicarbonate, 90%; fetal bovine serum, 10%; 37C.

### Experimental

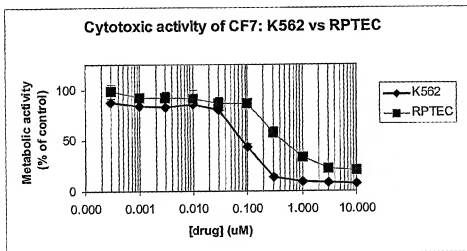
To K562 cells (suspension grown in DMEM media supplemented w/10% Fetal Bovine Serum (FBS) and 1mM HEPES; subcultured biweekly at 100K cells/ml) in a 96 well plate (0.1 ml medium; 2000 cells per well) were added various concentrations of 17-AAG (CF7) and the effects measured over a period of 3-6 days using an MTS assay protocol similar to that offered by Promega Corp (Madison, WI, US; cat# G5421).

The MTS assay is a colorimetric assay for determining the number of viable cells in proliferation, cytotoxicity or chemosensitivity assays. The CellTiter 96® AQueous Assay is composed of solutions of tetrazolium compound (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt; MTS) and an electron coupling reagent (phenazine methosulfate) PMS. MTS is bioreduced by cells into a formazan that is soluble in tissue culture medium. Barltrop et al. (1991) Bioorg. & Med. Chem. Lett. 1, 611. The absorbance of the formazan at 490nm can be measured directly from 96 well assay plates without additional processing. Cory et al. (1991) Cancer Commun. 3, 207; Riss, T.L. and Moravec, R.A. (1992) Mol. Biol. Cell 3 (Suppl.), 184a. The conversion of MTS into the aqueous soluble formazan is accomplished by dehydrogenase enzymes found in metabolically active cells. The quantity of formazan product as measured by the amount of 490nm absorbance is directly proportional to the number of living cells in culture.

Using the MTS assay, cytotoxicity (defined as "growth inhibition" and not necessarily versus renal proximal tubular endothelial cells (normal cells) was determined as shown in the following Tables. "Sem" refers to standard error of the mean, which is calculated as the standard deviation divided by the square root of the sample size; the numbers reflect triplicate replicates. Dilutions of the compounds were prepared in DMSO and straight DMSO was used as a control corresponding to 100% metabolic activity.

Conc (uM)	Metabolic Activity			
	K562	sem1	RPTEC	sem1
10.0000	7.89	0.56	20.10	2.64
3.0000	8.12	1.02	22.01	2.49
1.0000	9.51	0.59	34.01	0.19
0.3000	14.40	1.53	58.03	5.09
0.1000	44.06	2.76	86.46	1.51
0.0300	80.12	2.29	86.40	5.96
0.0100	85.94	0.06	91.81	8.22
0.0030	83.00	2.25	92.73	4.79

0.0010	83.81	0.73	92.26	2.97
0.0003	88.00	0.40	98.69	7.16

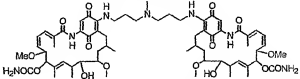
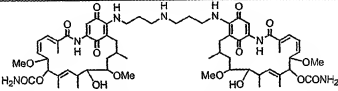
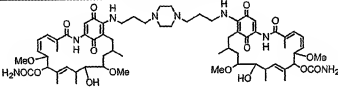
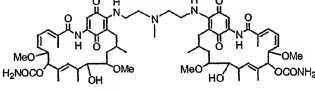
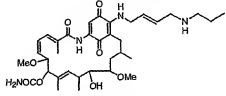


As demonstrated, the fusion protein cancer line K562 is more sensitive to the HSP90 inhibitor than is the normal cell line, RPTEC. It is expected that this will hold true for a variety of tumor cell lines versus a variety of normal cell lines.

In addition to the effects of 17-AAG on K562 versus RPTEC, the effects of a number of other putative HSP90 inhibitors and control compounds were tested side-by-side per the following Table, where "NEC" refers to no effective concentration.

Compound	RPTEC IC <sub>50</sub> (nM)	K562 IC <sub>50</sub> (nM)
CF7	400	70
DMSO	NEC	NEC
208	1000	50
237	4000	100
483	1000	70
481	4000	400

In the table, compound CF7 is the well known 17-AAG and compounds 207, 208, 237, 483, and 481 have the following formulas.

Compound #	Formula
208	 <p>a water soluble dimer</p>
237	 <p>a water soluble dimer</p>
207	 <p>a water soluble dimer</p>
483	 <p>a water soluble dimer</p>
481	 <p>a water soluble prodrug</p>

A separate study using the well known compound, radicicol, yielded results approximating those obtained for compound 237. Preparation of compounds 207, 208, 237, 483, and 481 is described in the following examples.

### Example 2:

#### Preparation of Compound #208

3,3'-diamino-N-methylpropylamine (1.32g, 9.1mmol) was added dropwise to a solution of Geldanamycin (10g, 17.83mmol) in DMSO (200ml) in a flame-dried flask under N<sub>2</sub> and stirred at room temperature. The reaction mixture was diluted with water after 12 hours. A precipitate was formed and filtered to give the crude product. The crude product was chromatographed by silica chromatography (5% CH<sub>3</sub>OH/CH<sub>2</sub>Cl<sub>2</sub>) to afford the desired dimer as a purple solid (8.92g, 7.2mmol). Yield: 81%; mp 153°C (dec.); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.95 (d, J = 7 Hz, 6H, 2CH<sub>3</sub>), 1.0 (d, J = 7 Hz, 6H, 2CH<sub>3</sub>), 1.69 (m, 4H, 2CH<sub>2</sub>), 1.74 (m, 4H, 2CH<sub>2</sub>), 1.76 (s, 6H, 2CH<sub>3</sub>), 1.83 (m, 2H, 2CH), 2.0 (s, 6H, 2CH<sub>3</sub>), 2.3 (s, 3H, N-CH<sub>3</sub>), 2.36 (dd, J = 14Hz, 2H, 2CH), 2.5 (m, 4H, 2CH<sub>2</sub>), 2.63 (d, 2H, 2CH), 2.75 (m, 2H, 2CH), 3.25 (s, 6H, 2OCH<sub>3</sub>), 3.35 (s, 6H, 2OCH<sub>3</sub>), 3.4 (m, 2H, 2CH), 3.50 (m, 4H, 2CH<sub>2</sub>), 3.68 (m, 2H, 2CH), 4.2 (Bs, 2H, OH), 4.3 (d, J = 10 Hz, 2H, 2CH), 4.8 (Bs, 4H, 2NH<sub>2</sub>), 5.19 (s, 2H, 2CH), 5.82 (t, J = 15 Hz, 2H, 2CH=), 5.89 (d, J = 10 Hz, 2H, 2CH=), 6.59 (t, J = 15 Hz, 2H, 2CH=), 6.92 (d, J = 10 Hz, 2H, 2CH=), 7.13 (t, 2H, 2NH), 7.24 (s, 2H, 2CH=), 9.21 (s, 2H, 2NH); MS (m/z) 1203 (M+H).

The corresponding HCl salt was prepared by the following method: an HCl solution in EtOH (5 ml, 0.123N) was added to a solution of compound #208 (1 gm as prepared above) in THF (15 ml) and EtOH (50 ml) at room temperature. The reaction mixture was stirred for 10 min. The salt was precipitated, filtered and washed with large amount of EtOH and dried in vacuo.

### Example 3:

#### Preparation of Compound #207

Compound #207 was prepared by the same method described in example 2 except that 1,4-bis (3-aminopropyl) piperazine was used instead of 3,3'-diamino-N-methylpropylamine. The pure purple product was obtained after column chromatography (silica gel); yield: 90%; mp 162°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.97 (d, J = 6.6 Hz, 6H, 2CH<sub>3</sub>), 1.0 (d, J = 6.6 Hz, 6H, 2CH<sub>3</sub>), 1.73 (m, 4H, 2CH<sub>2</sub>), 1.78 (m, 4H, 2CH<sub>2</sub>), 1.80 (s, 6H, 2CH<sub>3</sub>), 1.85 (m, 2H, 2CH), 2.0 (s, 6H, 2CH<sub>3</sub>), 2.4 (dd, J = 11Hz, 2H, 2CH), 2.55 (m, 8H, 4CH<sub>2</sub>), 2.67 (d, J = 15 Hz, 2H, 2CH), 2.63 (t, J = 10 Hz, 2H, 2CH), 2.78 (t, J = 6.5 Hz, 4H, 2CH<sub>2</sub>), 3.26 (s, 6H, 2OCH<sub>3</sub>), 3.38 (s, 6H, 2OCH<sub>3</sub>), 3.4 (m, 2H, 2CH), 3.60 (m, 4H, 2CH<sub>2</sub>), 3.75 (m, 2H, 2CH), 4.6 (d, J = 10 Hz, 2H, 2CH), 4.65 (Bs, 2H, 2OH), 4.8 (Bs, 4H, 2NH<sub>2</sub>), 5.19 (s, 2H, CH), 5.83 (t, J = 15 Hz, 2H, 2CH=), 5.89 (d, J = 10 Hz, 2H, 2CH=), 6.58 (t, J = 15 Hz, 2H, 2CH=), 6.94 (d, J = 10 Hz, 2H, 2CH=), 7.24 (s, 2H, 2CH=), 7.60 (m, 2H, 2NH), 9.20 (s, 2H, 2NH); MS (m/z) 1258 (M+H); The corresponding HCl salt was prepared by the same procedure as described in example 1.

**Example 4:****Preparation of Compound #237**

Compound #237 was prepared by the same method described in example 2 except that 3,3'-diamino-dipropylamine was used instead of 3,3'-diamino-N-methyldipropylamine. The pure purple product was obtained after flash chromatography (silica gel); yield: 93%; mp 165°C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) □ 0.97 (d, J = 6.6 Hz, 6H, 2CH<sub>3</sub>), 1.0 (d, J = 6.6 Hz, 6H, 2CH<sub>3</sub>), 1.72 (m, 4 H, 2 CH<sub>2</sub>), 1.78 (m, 4 H, 2CH<sub>2</sub>), 1.80 (s, 6 H, 2 CH<sub>3</sub>), 1.85 (m, 2H, 2CH), 2.0 (s, 6H, 2CH<sub>3</sub>), 2.4 (dd, J = 11Hz, 2H, 2CH), 2.67 (d, J = 15 Hz, 2H, 2CH), 2.63 (t, J = 10 HZ, 2H, 2CH), 2.78(t, J = 6.5 Hz, 4H, 2CH<sub>2</sub>), 3.26(s, 6H, 2OCH<sub>3</sub>), 3.38(s, 6H, 2OCH<sub>3</sub>), 3.4 (m, 2H, 2CH), 3.60 (m, 4H, 2CH<sub>2</sub>), 3.75(m, 2H, 2CH), 4.6( d, J = 10 Hz, 2H, 2CH), 4.65 (Bs, 2H, 2OH), 4.8(Bs, 4H, 2NH<sub>2</sub>), 5.19(s, 2H, 2CH), 5.83(t, J = 15 Hz, 2H, 2CH=), 5.89(d, J = 10 Hz, 2H, 2CH=), 6.58( t, J = 15 Hz, 2H, 2CH=), 6.94 (d, J = 10 Hz, 2H, 2CH=), 7.17 (m, 2H, 2NH ), 7.24(s, 2H, 2CH=), 9.20(s, 2H, 2NH); MS (m/z)1189 (M+H); The corresponding HCl salt was prepared by the same procedure as described in example 1.

**Example 5:****Preparation of Compound #483**

Compound #483 was prepared by the same method described in example 2 except that 2,2'-diamino-N-methyldiethylamine was used instead of 3,3'-diamino-N-methyldipropylamine. The pure purple product was obtained after flash chromatography; yield: 90%; mp 167-169 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) □ 0.95 (d, J = 7 Hz, 6H, 2CH<sub>3</sub>), 1.00 (d, J = 7 Hz, 6H, 2CH<sub>3</sub>), 1.85 (m, 4 H, 2CH<sub>2</sub>), 1.75 (s, 6 H, 2 CH<sub>3</sub>), 1.80 (m, 2H, 2CH), 2.0 (s, 6H, 2CH<sub>3</sub>), 2.30 (s, 3H, N-CH<sub>3</sub>), 2.30 (dd, J = 14Hz, 2H, 2CH), 2.5 (m, 4H, 2CH<sub>2</sub>), 2.63 (d, 2H, 2CH), 2.75(m, 2H, 2CH), 3.25(s, 6H, 2OCH<sub>3</sub>), 3.35(s, 6H, 2OCH<sub>3</sub>), 3.4 (m, 2H, 2CH), 3.50 (m, 4H, 2CH<sub>2</sub>), 3.68(m, 2H, 2CH), 4.2(Bs, 2H, OH), 4.30 (d, J = 10 Hz, 2H, 2CH), 4.8(Bs, 4H, 2NH<sub>2</sub>), 5.19 (s, 2H, 2CH), 5.82 (t, J = 15 Hz, 2H, 2CH=), 5.90 (d, J = 10 Hz, 2H, 2CH=), 6.59( t, J = 15 Hz, 2H, 2CH=), 6.92 (d, J = 10 Hz, 2H, 2CH=), 7.13 (t, 2H, 2NH ), 7.24 (s, 2H, 2CH=), 9.20 (s, 2H, 2NH); MS (m/z)1175 (M+H); ); The corresponding HCl salt was prepared by the same procedure as described in example 1.

**Example 6:****Preparation of Compound #481**

To 200 mg (0.357 mmol) of geldanamycin in 8 ml of dry THF in a flame-dried flask was added 91.6 mg (0.714 mmol) of N-propyl-1,4-diamino-2-butene drop-wise under nitrogen. The reaction mixture was stirred at room temperature for 4 h at which time TLC analysis indicated the reaction was complete. The solvent was removed by rotary evaporation and the crude material was chromatographed (5% CH<sub>3</sub>OH/CH<sub>2</sub>Cl<sub>2</sub> to 15% CH<sub>3</sub>OH/CH<sub>2</sub>Cl<sub>2</sub>) to afford the desired compound as a purple solid (150 mg, 0.228 mmol); yield: 64%; mp 131 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.97 (m, 9H, 3CH<sub>3</sub>), 1.52 (m, 2H, CH<sub>2</sub>), 1.72 (m, 3H, CH + CH<sub>2</sub>), 1.80 (s, 3 H, CH<sub>3</sub>), 2.0 (s, 3H, CH<sub>3</sub>), 2.38 (dd, J = 11Hz, 1H, CH), 2.72 (m, 4H, 2CH, CH<sub>2</sub>), 3.26 (s, 3H, OCH<sub>3</sub>), 3.38 (s, 3H, OCH<sub>3</sub>), 3.46 (m, H, CH), 3.6 (m, H, CH), 4.18 (m, 4H, 2CH<sub>2</sub>), 4.34 (d, J = 10 Hz, 1H, CH), 4.8 (bs, 2H, NH<sub>2</sub>), 5.19 (s, 1H, CH), 5.88 (m, 4H, 4CH=), 6.38 (m, 1H, NH), 6.61 (t, J = 15 Hz, 1H, CH=), 6.94 (d, J = 10 Hz, 1H, CH=), 7.30 (s, H, CH=), 9.16 (s, H, NH); MS (m/z) 658 (M+H). The corresponding HCl salt was prepared by the same procedure as described in example 1.

\* \* \*

Various patents, publications, and formulations are within the levels of ordinary skill in the art to which the invention pertains. All documents including the sequence listing cited in this disclosure are incorporated by reference to the same extent as if each reference had been incorporated by reference in its entirety individually, although none is admitted to be prior art.

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The methods and compositions described herein as presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art, are encompassed within the spirit of the invention, and are defined by the scope of the claims.

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention. Thus, such additional embodiments are within the scope of the present invention and the following claims.



The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising," "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions  
5 which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments, optional features,  
10 modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the description and the appended claims.

In addition, where features or aspects of the invention are described in terms of Markush groups or other grouping of alternatives, those skilled in the art will recognize that the invention is  
15 also thereby described in terms of any individual member or subgroup of members of the Markush group or other group, and exclusions of individual members as appropriate.

## Claims

We claim:

1. A method of treating a patient having a genetically-defined disease characterized by a chromosomal aberration that yields an oncogenic fusion protein, comprising:
  - 5 providing a cell, tissue, or fluid sample of a patient suspected of having said genetically-defined disease;  
  
identifying one or more characteristics indicative of said disease in or on said cell, tissue, or fluid sample; and  
  
administering to said patient a pharmaceutically effective amount of an HSP90-  
10 inhibiting compound.
  2. The method of claim 1, wherein said compound is an ansamycin.
  3. The method of claim 2, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, and macbecin.
  4. The method of claim 2, wherein said ansamycin is 17-AAG.
  - 15 5. The method of claim 1, wherein said compound is a compound that binds into the ATP-binding site of a HSP90.
  - 6 The method of claim 5 wherein said compound is radicicol or an analog thereof.
  7. The method of claim 1 wherein said identifying comprises using PCR or LCR to identify a nucleic acid encoding said oncogenic fusion protein.
  - 20 8. The method of claim 1 wherein said identifying comprises using an antibody to identify said fusion protein.
  9. The method of claim 1 wherein said identifying comprises using a cytochemical technique.
  10. The method of claim 9 wherein said cytochemical technique employs nucleic acid  
25 hybridization.

11. The method of claim 10 wherein said cytochemical technique is FISH.
12. The method of claim 1 wherein said disease is a hematopoietic disorder.
13. The method of claim 11 wherein said hematopoietic disorder is selected from the group consisting of a T or B cell lymphoma, CML, APL, ALL, AML, NHL, and CMML.
- 5 14. The method of claim 1 wherein said disease is characterized by a solid tumor.
15. The method of claim 14 wherein said solid tumor is selected from the group consisting of papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, synovial sarcoma.
- 10 16. The method of claim 1 wherein said fusion protein contains one or more functional domains or portions thereof selected from the group consisting of kinases and DNA binding motifs.
17. The method of claim 12 or 13 wherein said administering employs an *ex vivo* procedure.
- 15 18. The method of claim 14 wherein said administering is intralesional.
19. The method of claim 1 wherein said administering is parenteral.
20. The method of claim 1 wherein said HSP90-inhibiting compound has an  $IC_{50}$  at least two-fold higher for cells that do not have characteristics indicative of said genetically-defined proliferative disorder relative to those cells that do have such
- 20 characteristics.
21. The method of claim 1 wherein said HSP90-inhibiting compound has an  $IC_{50}$  at least five-fold higher for cells that do not have characteristics indicative of said genetically-defined proliferative disorder relative to those cells that do have such characteristics.

22. The method of claim 1 wherein said HSP90-inhibiting compound has an  $IC_{50}$  at least ten-fold higher for cells that do not have characteristics indicative of said genetically-defined proliferative disorder relative to those cells that do have such characteristics.

23. The method of claim 1 wherein cells of said patient are monitored *in vitro* for sensitivity prior to administration of said compound to said patient.

24. The method of claim 1 wherein said non-random chromosomal aberration is a translocation.

25. The method of claim 1 wherein said non-random chromosomal aberration is a inversion.

26. The method of claim 1 wherein said non-random chromosomal aberration is a deletion.

27. The method of claim 1 wherein said non-random chromosomal aberration is selected from the group consisting of inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9; 12)(q34;p13), del(12p), t(15; 17)(q22;q12), t(11; 17)(q23;q12), t(16; 16)(p13;q22), inv(16)(p13;q22), t(9; 11)(p22;q23), t(1; 22)(p13;q13), t(3; 3)(q21;q26), inv(3)(q21q26), t(3; 5)(q21;q31), t(3; 5)(q25;q34), t(7; 11)(p15;p15), t(8; 16)(p11;p13), t(9; 12)(q34;p13), t(12; 22)(p13;q13), del(5q), del(7q), del(20q), t(11q23), t(12; 21)(p13;q22), t(5; 12)(q31;p13), t(1; 12)(q25;p13), t(12; 15)(p13;q25), t(1; 12)(q21;p13), t(12; 21)(q13;p32), and t(5; 7)(q33;q11.2)).

28. The method of claim 1 wherein said non-random chromosomal aberration is a t(9; 22)(q34; q11) optionally characterized by and comprising a sequence selected from any one of SEQ ID NOs 15-26 or a homolog, isoform, or allelic variation thereof.

29. A method of treating cancerous cells in a heterogeneous population of cells, said heterogeneous population comprising both cancerous and noncancerous, and said

cancerous cells characterized by fusion proteins not found in said noncancerous cells, said method comprising:

administering to said heterogeneous population of cells a pharmaceutically effective amount of an HSP90-inhibiting compound.

- 5 30. The method of claim 29 wherein said compound has an  $IC_{50}$  that is at least five-fold lower for said cancerous cells than for said noncancerous cells within said heterogeneous population, and wherein said pharmaceutically effective amount administered is about one half or less of the  $IC_{50}$  of said noncancerous cells.
- 10 31. The method of claim 29 wherein said compound has an  $IC_{50}$  that is at least ten-fold lower for said cancerous cells than for said noncancerous cells within said heterogeneous population, and wherein said pharmaceutically effective amount administered is about one half or less of the  $IC_{50}$  of said noncancerous cells.
32. The method of any of claims 29-31, wherein said compound is an ansamycin.
- 15 33. The method of claim 32, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, and macbecin.
34. The method of claim 33, wherein said ansamycin is 17-AAG.
35. The method of any of claims 29-31 wherein said HSP90-inhibiting compound is a compound that binds the ATP-binding site of a HSP90.
- 20 36. The method of any of claims 29-31 wherein said cancerous cells are leukemic cells.
37. The method of claim 36 wherein said leukemic cells are selected from the group consisting of a T or B cell lymphoma, CML, APL, ALL, AML, NHL, and CMML.
- 25 38. The method of any of claims 29-31 wherein said treatment is monitored using one or more techniques selected from the group consisting of PCR, antibody staining, and nucleic acid hybridization, and wherein said techniques are selective for the presence of cancerous cells.

The method of any of claims 29-31 wherein said genetically-defined proliferative disorder is a solid tumor.

40. The method of claim 39 wherein said solid tumor is selected from the group consisting of papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma, rhabdomyosarcoma, and synovial sarcoma.

41. The method of any of claims 29-31 wherein said fusion protein contains one or more functional domains selected from the group consisting of kinases and DNA binding motifs.

42. The method of any of claims 29-31 wherein said administering employs an *ex vivo* procedure.

43. The method of any of claims 29-31 wherein said administering is intralesional.

44. The method of any of claims 29-31 wherein said administering is parenteral.

45. The method of claim 29 wherein said fusion protein arises from a chromosomal translocation.

46. The method of claim 29 wherein said fusion protein arises from a chromosomal inversion.

47. The method of claim 29 wherein said fusion protein arises from a chromosomal deletion.

48. The method of claim 29 wherein said fusion protein is generated from a non-random chromosomal aberration selected from the group consisting of inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9; 12)(q34;p13), del(12p), t(15; 17)(q22;q12), t(11; 17)(q23;q12), t(16; 16)(p13;q22), inv(16)(p13;q22), t(9; 11)(p22;q23), t(1; 22)(p13;q13), t(3; 3)(q21;q26), inv(3)(q21q26), t(3; 5)(q21;q31), t(3; 5)(q25;q34), t(7; 11)(p15;p15), t(8; 16)(p11;p13), t(9; 12)(q34;p13), t(12; 22)(p13;q13),

39. The method of any of claims 29-31 wherein said genetically-defined proliferative disorder is a solid tumor.
40. The method of claim 39 wherein said solid tumor is selected from the group consisting of papillary thyroid carcinoma, Ewing's sarcoma, melanoma, liposarcoma,  
5 rhabdomyosarcoma, and synovial sarcoma.
41. The method of any of claims 29-31 wherein said fusion protein contains one or more functional domains selected from the group consisting of kinases and DNA binding motifs.
42. The method of any of claims 29-31 wherein said administering employs an *ex vivo*  
10 procedure.
43. The method of any of claims 29-31 wherein said administering is intralesional.
44. The method of any of claims 29-31 wherein said administering is parenteral.
45. The method of claim 29 wherein said fusion protein arises from a chromosomal translocation.
- 15 46. The method of claim 29 wherein said fusion protein arises from a chromosomal inversion.
47. The method of claim 29 wherein said fusion protein arises from a chromosomal deletion.
48. The method of claim 29 wherein said fusion protein is generated from a non-  
20 random chromosomal aberration selected from the group consisting of inv14 (q11; q32), t(9; 22)(q34; q11), t(1; 19)(q23; p13.3), t(17; 19)(q22; p13), t(15; 17)(q21-q11-22), t(11; 17)(q23; q21.1), t(4; 11)(q21; q23), t(9; 11)(q21; q23), t(11; 19)(q23; p13), t(X; 11)(q13; q23), t(1; 11)(p32; q23), t(6; 11)(q27; q23), t(11; 17)(q23; q21), t(8; 21)(q22; q22), t(3; 21)(q26; q22), 5(16; 21)(p11; q22), t(6; 9)(p23; q34), t(4; 16)(q26; p13), inv(2; 2)(p13; p11.2-14), inv(16)(p13q22), t(5; 12)(q33; p13), t(2; 5)(2p23; q35), t(9; 12)(q34;p13),  
25 del(12p), t(15; 17)(q22; q12), t(11; 17)(q23; q12), t(16; 16)(p13; q22), inv(16)(p13; q22), t(9; 11)(p22; q23), t(1; 22)(p13; q13), t(3; 3)(q21; q26), inv(3)(q21q26), t(3; 5)(q21; q31), t(3; 5)(q25; q34), t(7; 11)(p15; p15), t(8; 16)(p11; p13), t(9; 12)(q34; p13), t(12; 22)(p13; q13),

del(5q), del(7q), del(20q), t(11q23), t(12;21)(p13;q22), t(5;12)(q31;p13), t(1;12)(q25;p13), t(12;15)(p13;q25), t(1;12)(q21;p13), t(12;21)(q13;p32), and t(5;7)(q33;q11.2)).

49. The method of claim 29 wherein said non-random chromosomal aberration is t(9;22)(q34;q11).

5 50. The method of claim 1 or 29 wherein said fusion protein has a heightened dependence on HSP90.

51. The method of claim 20 or 29 wherein said HSP90-inhibiting compound has an IC<sub>50</sub> that is lower for cancerous cells than for noncancerous cells.

52. The method of claim 5 or 35 wherein said inhibitor is a synthetic analog of geldanamycin.

10 53. A method of treating a patient having a proliferative disease associated with a mutant protein or cellular protein isoform dependent on HSP90, comprising:

providing a cell, tissue, or fluid sample of a patient suspected of having said proliferative disease;

identifying in said cell, tissue, or fluid sample one or more characteristics

15 indicative of said mutant protein or cellular protein isoform; and

administering to said patient a pharmaceutically effective amount of an HSP90-inhibiting compound.

54. The method of claim 53 wherein said mutant protein or cellular protein isoform is selected from the group consisting of src, RET, p53, p51, p63, p73, and homologs and  
20 allelic variations thereof.

55. The method of claim 53 wherein said mutant protein or cellular protein isoform is a dominant negative mutant.

56. The method of claim 53 wherein said mutant protein or cellular protein isoform is a human p53 selected from the group consisting of N239S, C176R, and R213\*, Y236delta,  
25 C176Y, M133T, G245D, E258K, 1-293delta, G245C, R248W, E258K, R282W, R175H,



R280K, V143A, R175H, P177S, H178P, H179R, R181P, 238-9delta, G245S, G245D, M246R, R248Q, R249S, R273H, R273C, R273L, and D281Y.

57. The method of claim 53 wherein said mutant protein or cellular protein isoform is a dominant positive mutant.

5 58. The method of claim 57 wherein said mutant protein or cellular protein isoform is a C176Y mutant.

59. The method of claim 53 wherein said patient is heterozygous for said mutant protein or cellular protein isoform.

60. The method of claim 59 wherein said mutant protein or cellular protein isoform is p53 and wherein said proliferative disease is rheumatoid arthritis.

61. The method of claim 53, wherein said compound is an ansamycin.

62. The method of claim 61, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, and macbecin.

63. The method of claim 62, wherein said ansamycin is 17-AAG.

15 64. The method of claim 53, wherein said inhibitor is a compound that binds into the ATP-binding site of a HSP90.

65. The method of claim 64 wherein said compound is radicicol or an analog thereof.

66. The method of claim 53 wherein said identifying comprises using at least one technique selected from the group consisting of nucleic acid hybridization, PCR, LCR, antibody staining, and immunoprecipitation to determine the presence of said mutant  
20 protein or cellular protein isoform.

67. The method of claim 53 wherein said administering employs an *ex vivo* procedure.

68. The method of claim 53 wherein said administering is intralesional.

69. The method of claim 53 wherein said administering is parenteral.

70. The method of claim 53 wherein said HSP90-inhibiting compound has an  $IC_{50}$  at least two-fold higher for cells that do not have characteristics indicative of said mutant protein or cellular protein isoform relative to those cells that do have such characteristics.

71. The method of claim 53 wherein said HSP90-inhibiting compound has an  $IC_{50}$  at least ten-fold higher for cells that do not have characteristics indicative of said mutant protein or cellular protein isoform relative to those cells that do have such characteristics.

72. The method of claim 53 wherein cells of said patient are monitored *in vitro* for sensitivity prior to administration of said compound to said patient.

73. A method of selectively treating cells that express a mutant protein or cellular protein isoform that gives rise to a proliferative disorder dependent on HSP90, said method comprising:

providing a population of cells in which at least some of said population express a mutant protein or cellular protein isoform that is differentially dependent on HSP90 for effect and gives rise to a proliferative disorder, and

administering to said population a pharmaceutically effective amount of an HSP90-inhibiting compound.

74. The method of claim 73 wherein said compound has an  $IC_{50}$  that is at least five-fold lower for said cells that express said mutant protein or cellular protein isoform than for those cells that do not, and wherein said pharmaceutically effective amount administered is about one half or less of the  $IC_{50}$  of cells that do not express said mutant protein or cellular protein isoform.

75. The method of claim 73 wherein said compound has an  $IC_{50}$  that is at least ten-fold lower for said cells that express said mutant protein or cellular protein isoform than for those cells that do not, and wherein said pharmaceutically effective amount administered is about one half or less of the  $IC_{50}$  of cells that do not express said mutant protein or cellular protein isoform..

76. The method according to any of claims 73-75, wherein said compound is an ansamycin.

77. The method of claim 76, wherein said ansamycin is selected from the group consisting of geldanamycin, 17-AAG, herbimycin A, or macbecin.
78. The method of claim 77, wherein said ansamycin is 17-AAG.
79. The method of any of claims 73-75, wherein said compound is a compound that  
5 binds the ATP-binding site of a HSP90.
80. The method of claim 79 wherein said compound is radicicol or an analog thereof.
81. The method of any of claims 73-75 wherein said treatment is monitored using one or more techniques selected from the group consisting of PCR, LCR, nucleic acid hybridization, antibody labeling, and immunoprecipitation, and wherein said techniques  
10 are selective for the presence of said mutant protein or cellular protein isoform.
82. The method of any of claims 73-75 wherein said administering employs an *ex vivo* procedure.
83. The method of any of claims 73-75 wherein said administering is intralesional.
84. The method of any of claims 73-75 wherein said administering is parenteral.
- 15 85. The method of claim 76 wherein said HSP90-inhibiting compound has an  $IC_{50}$  that is lower for cells expressing the mutant protein or cellular protein isoform than for cells that do not express said mutant protein or cellular protein isoform.
86. The method of claim 64 or 73 wherein said inhibitor is a synthetic analogue of geldanamycin.
- 20 87. The method of claim 73 wherein said mutant protein or cellular protein isoform is selected from the group consisting of src, RET, p53, p51, p63, p73, and homologs and allelic variations thereof.
88. The method of claim 73 wherein said mutant protein or cellular protein isoform is a dominant negative mutant.

89. The method of claim 88 wherein said mutant protein or cellular protein isoform is a human p53 selected from the group consisting of N239S, C176R, and R213\*, Y236delta, C174Y, M133T, G245D, E258K, 1-293delta, G245C, R248W, E258K, R282W, R175H, R280K, V143A, R175H, P177S, H178P, H179R, R181P, 238-9delta, G245S, G245D,  
5 M246R, R248Q, R249S, R273H, R273C, R273L, and D281Y.
90. The method of claim 73 wherein said mutant protein or cellular protein isoform is a dominant positive mutant.
91. The method of claim 90 wherein said mutant protein or cellular protein isoform is C176Y human p53, or a homolog thereof.
- 10 92. The method of claim 73 wherein said cells that express a mutant protein or cellular protein isoform are heterozygous for said mutant protein or cellular protein isoform.
93. The method of claim 92 wherein said mutant protein or cellular protein isoform is p53 and wherein said proliferative disease is rheumatoid arthritis or a cancer.

## FIGURE 1

Type of Aberration	Background Literature	Affected Gene(s)	Protein Domain	Fusion Protein	Disease
t(9;22)(q34;q11)	de Klein, A. et al. Nature 300, 765-767 (1982)	<i>CABL</i> (9q34) <i>BCL</i> (22q11)	tyrosine kinase serine kinase	serine + tyrosine kinase	CML/ALL
inv14 (q11; q32)	Baer, R., Chen, K.-C., Smith, S. D. & Rabbits, T. H. Cell 43, 705-713 (1983); Denny, C. T. et al. Nature 320, 549-551 (1986)	<i>TCR-α</i> (14q11) <i>VH</i> (14q32)	TCR-α Ig VH	VH-TCR-α	T/B-cell lymphoma
t(1;19)(q23;p13.3)	Kamps, M. P., Murru, C., Sun, X.-H. & Baltimore, D. Cell 60, 547-555 (1990); Nourse, J. et al. Cell 60, 535-545 (1990)	<i>PBX1</i> (1q23) <i>E2A</i> (19p13.3)	HD AD-b-HLH	AD + HD	pre-B-ALL
t(17;19)(q22;p13)	Hunger, S. P., Ohyashiki, K., Toyama, K. & Cleary, M. L. Genes Dev. 6, 1608-1620 (1992); Imbub, I. et al. Science 257, 531-534 (1992)	<i>HLF</i> (17q22) <i>E2A</i> (19p13)	bZIP AD-b-HLH	AD + bZIP	pro-B-ALL
t(15;17)(q21-q11-22)	Gilliland, E. F. & Solomon, E. Sem. Cancer Biol. 4, 359-368 (1993)	<i>PML</i> (15Q21) <i>RAR4</i> (17q21)	Zinc-finger Retinoic acid receptor-α	Zinc-finger + RAR DNA and ligand binding	APL
t(11;17)(q23;q21.1)	Chen, Z. et al. EMBO J. 12, 1161-1167 (1993)	<i>PLZF</i> (11q23) <i>RAR4</i> (17q21)	Zinc-finger Retinoic acid receptorα	Zn-finger + RAR DNA and ligand binding	APL
t(4;11)(q21;q23)	Djabali, M. et al. Nature Genet. 2, 113-118 (1992); Gu, Y. et al. Cell 71, 701-708 (1992)	<i>MLL</i> (11q23) <i>AF4</i> (4q21)	A-T' hook/Zn-finger Ser-Pro rich	A-T' hook + (Ser-pro)	ALL/preB- ALL/ ANLL
t(9;11)(q21;q23)	Nakamura, T. et al. Proc. natl. Acad. Sci. U.S.A. 90, 4631-4635 (1993); Lida, S. et al. Oncogene 8, 3085-3092 (1993)	<i>MLL</i> (11q23) <i>AF9/MLL73</i> (9p22)	A-T' hook/Zn-finger Ser-Pro rich	A-T' hook + (Ser-Pro)	ALL/preB- ALL/ ANLL
t(11;19)(q23;p13)	Trachuk, D. C., Kohler, S. & Cleary, M. L. Cell 71, 691-700 (1992); Yamamoto, K. et al. Oncogene 8, 2617-2625 (1993)	<i>MLL</i> (11q23) <i>ENL</i> (19p13)	A-T' hook/Zn-finger Ser-Pro rich	A-T' hook + Ser-Pro	pre-B-ALL/ T-ALL/ ANLL

FIGURE 1 (Cont'd)

Type of Aberration	Background Literature	Affected Gene(s)	Protein Domain	Fusion Protein	Disease
t(X;11)(q13;q23)	Corral, J. et al. Proc. natn. Acad. Sci. U.S.A. 90, 8538-8542 (1993)	<i>MLL</i> (11q23) <i>AFX1</i> (2q13)	A-T hook/Zn-finger Ser-Pro rich	A-T hook + (Ser-Pro)	T-ALL
t(1;11)(p32;q23)	Bernard, O. A., Manchauffe, M., Meucci, C., Van Den Berghe, H. & Berger, R. Oncogene 9, 1039-1045 (1994)	<i>MLL</i> (11q23) <i>AF1P</i> (1p32)	A-T hook/Zn-finger Eps-15 homologue	A-T hook +	ALL
t(6;11)(q27;q23)	Prasac, R. et al. Cancer Res. 53, 5624-5628 (1993)	<i>MLL</i> (11q23) <i>AF6</i> (6q27)	A-T hook/Zn-finger myosin homologue	A-T hook +	ALL
t(1;17)(q23;q21)	Prasac, R. et al. Proc. natn. Acad. Sci. U.S.A. 91, 8107-8111 (1994)	<i>MLL</i> (11q23) <i>AF17</i> (1p21)	A-T hook/Zn-finger Cys-rich/leucine zipper	A-T hook + leucine zipper	AML
t(8;21)(q22;q22)	Ohki, M. Sem. Cancer Biol. 4, 369-376 (1993)	<i>AML1/CEBFA</i> (21q22) <i>ETO/MTG8</i> (8q22)	DNA binding/runt homology Zn-finger	DNA binding + Zn-fingers	AML
t(3;21)(q28;q22)	Mitani, K. et al. EMBO J. 13, 504-510 (1994)	<i>AML1</i> (21q22) <i>EVI-1</i> (3q26)	DNA binding Zn-finger	DNA binding + Zn-fingers	CML
t(3;21)(q26;q22)	Nacifora, G., Begy, C. R., Erickson, P., Drackin, H. A. & Rowley, J. D. Proc. natn. Acad. Sci. U.S.A. 90, 7784-7788 (1993)	<i>AML1</i> (21q22) <i>EAP</i> (3q26)	DNA binding Sn protein	DNA binding + out-of-frame EAP	Myelo-dysplasia
5(16;21)(p11;q22)	Shimizu, K. et al. Proc. natn. Acad. Sci. U.S.A. 90, 10280-10284 (1993)	<i>FUS</i> (16p11) <i>ERG</i> (21q22)	Gln-Ser-Tyr(Gly-rich)/RNA binding Ets-like DNA binding	Gln-Ser-Tyr + DNA binding	Myeloid
t(6;9)(p23;q34)	von Lindern, M. et al. Molec. Cell Biol. 12, 1687-1697 (1992)	<i>DEK</i> (6p23) <i>CAN</i> (9q34)	unknown ZIP	ZIP+	AML
9;9?	von Lindern, M., Freeman, D., van Baasi, S., Acrianien, H. & Grosfeld, G. Genes Chrom. Cancer 5, 227-234 (1992)	<i>SET</i> (9q34) <i>CAN</i> (9p34)	ZIP	ZIP+	AUL
t(4;16)(q26;p13)	Laabi, Y. et al. EMBO J. 11, 3897-3904 (1992)	<i>IL-2</i> (4q26) <i>RCM</i> (16p13.1)	IL2 TM domain	IL-2/TM	T-lymphoma

FIGURE 1 (Cont'd)

<u>Type of Aberration</u>	<u>Background Literature</u>	<u>Affected Gene(s)</u>	<u>Protein Domain</u>	<u>Fusion Protein</u>	<u>Disease</u>
inv(2;2)(p13; p1.2-1.4)	Lu, D. et al. <i>Oncogene</i> 6, 1235-1241 (1991)	<i>REL</i> (2p13) <i>NRG</i> (2p11.2-1.4)	DNA binding-activator not known	DNA binding +	NHL
inv(16)(p13q22)	Liu, P. et al. <i>Science</i> 261, 1041-1044 (1993)	Myosin MYH11 (16p13) CBF- $\beta$ (16q22)		DNA binding?	AML
t(5;12)(q33; p13)	Golub, T. R., Barker, G. F., Lovett, M. & Gilliland, D. G. <i>Cell</i> 77, 307-316 (1994)	<i>PDGF-<math>\beta</math></i> (5q33) <i>TEL</i> (12p13)	Receptor kinase Ets-like DNA binding	Kinase + DNA binding	CML
t(2;5)(p23; q5)	Morris, S. W. et al. <i>Science</i> 263, 1281-1284 (1994)	<i>NPM</i> (5q35) <i>ALK</i> (2p23)	Nuclear phosphoprotein Tyrosine kinase	N terminus NPM + kinase	NHL
t(11;22)(q24; q12)	Delattre, O. et al. <i>Nature</i> 359, 162-165 (1992)	<i>FLII</i> (11q24) <i>EWS</i> (22q12)	Ets-like DNA binding Gin-Ser-Tyr/Gly-rich/RNA binding	Gin-Ser-Tyr + DNA binding	Ewing's sarcoma
inv10(q11.2; q21)	Pierotti, M. A. et al. <i>Proc. natl. Acad. Sci. U.S.A.</i> 89, 1616-1620 (1992)	<i>RET</i> (10q11.2) <i>D10S170</i> (q21)	tyrosine kinase uncharacterized	Unk + tyrosine kinase	Papillary thyroid carcinoma
t(12;22)(q13; q12)	Zucman, J. et al. <i>Nature Genet.</i> 4, 341-345 (1993)	<i>ATF7</i> (12q13) <i>EWS</i> (22q12)	bZIP Gin-Ser-Tyr/Gly-rich/RNA binding	Gin-Ser-Tyr + bZIP	a melanoma
t(12;16)(q13; p11)	Crozat, A., Anan, P., Mandahl, N. & Ron, D. <i>Nature</i> 363, 640-644 (1993); Rabbitts, T. H.; Forster, A., Larson, R. & Nathanael, P. <i>Nature Genet.</i> 4, 175-180 (1993)	<i>CHOP</i> (12q13) <i>FUS</i> (16p11)	(DNA binding)/ZIP Gin-Ser-Tyr/Gly-rich/RNA binding	Gin-Ser-Tyr +(DNA binding)/ZIP	Liposarcoma
t(2;13)(q35; q14)	Ben-David, Y., Giddens, E. B., Letwin, K. & Bernstein, A. <i>Genes Dev.</i> 5, 908-918 (1991)	<i>PAX3</i> (2q35) <i>FKBP</i> (13q14)	Paired box/homeodomain Forkhead domain	PB/HD +DNA binding	Rhabdomyosarcoma
t(X;18)(p11.2;q11.2)	Clark, J. et al. <i>Nature Genet.</i> 7, 502-5087 (1994)	<i>SYT</i> (18q11.2) <i>SSX</i> (Xp11.2)	None identified None identified		Synovial sarcoma

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## SEQUENCE LISTING

&lt;110&gt; CONFORMA THERAPEUTICS CORP.

<120> METHODS FOR TREATING GENETICALLY-DEFINED PROLIFERATIVE  
DISORDERS WITH HSP90 INHIBITORS

&lt;130&gt; 031164.0010W0

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&lt;150&gt; 60/272,751

&lt;151&gt; 2001-03-01

&lt;160&gt; 330

&lt;170&gt; PatentIn Ver. 2.1

&lt;210&gt; 1

&lt;211&gt; 46

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

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35 40 45

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&lt;210&gt; 3

&lt;211&gt; 561

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 3

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accaactcgt ggtgaaact ccagactgtc cacagcttc cgctgacct caataaggaa 120  
gatgatgagt ctccggggtt ctatgggttt ctgaatgtca tgcctccact agccactgga 180  
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tcaggccat gcagatgaag ccatatttac ctttgtgata ttggggctga tcttgagct 300  
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tcacctcgta tctgtactcg taactgctat ttctaggcga attgtcccoct ttctcctccc 420
tcttccctca tctccctctc tctcttgccct ggctgacacc aggaaggagg agtttttttt 480
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 Phe Gln Met Val Asp Glu Leu Glu Ala Val Pro Asn Ile Pro Leu Val  
 35 40 45  
 Pro Asp Glu Glu Leu Asn Ala Leu Lys Ile Lys Ile Ser Gln Ile Lys  
 50 55 60  
 Ser Asp Ile Gln Arg Glu Lys Arg Ala Asn Lys Gly Ser Lys Ala Thr  
 65 70 75 80  
 Glu Arg Leu Lys Lys Lys Leu Ser Glu Gln Glu Ser Leu Leu Leu Leu  
 85 90 95  
 Met Ser Pro Ser Met Ala Phe Arg Val His Ser Arg Asn Gly Lys Ser  
 100 105 110  
 Tyr Thr Phe Leu Ile Ser Ser Asp Tyr Glu Arg Ala Glu Trp Arg Glu  
 115 120 125  
 Asn Ile Arg Glu Gln Gln Lys Lys Cys Phe Arg Ser Phe Ser Leu Ala  
 130 135 140  
 Ser Val Glu Leu Gln Met Leu Thr Asn Ser Cys Val Lys Leu Gln Thr  
 145 150 155 160  
 Val His Ser Ile Pro Leu Thr Ile Asn Lys Glu Asp Asp Glu Ser Pro  
 165 170 175  
 Gly Leu Tyr Gly Phe Leu Asn Val Ile Val His Ser Ala Thr Gly Phe  
 180 185 190  
 Lys Gln Ser Ser Lys Leu Gln Arg Pro Val Ala Ser Asp Phe Glu Pro  
 195 200 205  
 Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys Glu Asn Leu Leu  
 210 215 220  
 Ala Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val Ala Leu Tyr Asp  
 225 230 235 240  
 Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr Lys Gly Glu Lys

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245

250

255

Leu Arg Val Leu Gly Tyr Asn His Asn Gly Glu Trp Cys Glu Ala Gln  
 260 265 270

Thr Lys Asn Gly Lys Gly Trp Val Pro Ser Asn Tyr  
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&lt;211&gt; 854

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&lt;213&gt; Homo sapiens

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 gcagtgcccc acatccccctt gggtccccgat gaggagctga acgctttgaa gatcaagatc 180  
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&lt;211&gt; 468

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 6

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 gggccagtag catctgactt tgagcctcag ggtctgagtg aagccgctcg ttggaactcc 180  
 aagggaaaac ttctcgtcgg acccagtgaa aatgacccca accttttctg tgcactgtat 240  
 gattttgttg ccagtgaggga taacactcta agcataacta aaggtgaaaa gctccgggtc 300  
 ttaggctata atcacaatgg ggaatggtgt gaagcccaaa ccaaaaatgg ccaaggctgg 360  
 gtccacagca actacatcac gccagtcac agtctggaga aacactcctg gtaccactcg 420  
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&lt;210&gt; 7

&lt;211&gt; 225

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 7

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Gly Ser Lys Ala Thr Glu Arg Leu Lys Lys Lys Leu Ser Glu Gln Glu

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Ser Leu Leu Leu Met	Ser Pro Ser Met Ala Phe Arg Val His Ser	
35	40	45
Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile Ser Ser Asp Tyr Glu Arg		
50	55	60
Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln Gln Lys Lys Cys Phe Arg		
65	70	75
Ser Phe Ser Leu Ala Ser Val Glu Leu Gln Met Leu Thr Asn Ser Cys		
85	90	95
Val Lys Leu Gln Thr Val His Ser Ile Pro Leu Thr Ile Asn Lys Glu		
100	105	110
Asp Asp Glu Ser Pro Gly Leu Tyr Gly Phe Leu Asn Val Ile Val His		
115	120	125
Ser Ala Thr Gly Phe Lys Gln Ser Ser Lys Leu Gln Arg Pro Val Ala		
130	135	140
Ser Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser		
145	150	155
Lys Glu Asn Leu Leu Ala Ala Pro Ser Glu Asn Asp Pro Asn Leu Phe		
165	170	175
Val Ala Leu Tyr Asp Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile		
180	185	190
Thr Lys Gly Glu Lys Leu Arg Val Leu Gly Tyr Asn His Asn Gly Glu		
195	200	205
Trp Cys Glu Ala Gln Thr Lys Ile Gly Gln Gly Trp Val Pro Ser Asn		
210	215	220

Tyr  
225

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 ccagcatggc cttcagggtg cacagccgca acggcaagag ttacacgttc ctgatctcct 180  
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 agcggccagt agcatctgac tttagcctc agggctctgag tgaagccgct cggtggaact 480  
 ccaaggaaaa ccttctcgtc gcacccagtg aaatgaccc caaccttttc gttgcactgt 540  
 atgattttgt ggccagtga gataaacctc taagcataac taaaggtgaa aagctccggg 600

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tcttaggcta taatcacaat ggggaatggt gtgaagccca aacccaaatt ggccaaggct 660  
 gggttccaag caactacat 679

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 Val His Ser Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile Ser Ser Asp  
 35 40 45  
 Tyr Glu Arg Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln Gln Lys Lys  
 50 55 60  
 Cys Phe Arg Ser Phe Ser Leu Thr Ser Val Glu Leu Gln Met Leu Thr  
 65 70 75 80  
 Asn Ser Cys Val Lys Leu Gln Thr Val His Ser Ile Pro Leu Thr Ile  
 85 90 95  
 Asn Lys Glu Asp Asp Glu Ser Pro Gly Leu Tyr Gly Phe Leu Asn Val  
 100 105 110  
 Ile Val His Ser Ala Thr Gly Phe Lys Gln Ser Ser Lys Ala Leu Gln  
 115 120 125  
 Arg Pro Val Ala Ser Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala  
 130 135 140  
 Arg Trp Asn Ser Lys Glu Asn Leu Leu Ala Gly Pro Ser Glu Asn Asp  
 145 150 155 160  
 Pro Asn Leu Phe Val Ala Leu Tyr Asp Phe Val Ala Ser Gly Asp Asn  
 165 170 175  
 Thr Leu Ser Ile Thr Lys Gly Glu Lys Leu Arg Val Leu Gly Tyr Asn  
 180 185 190  
 His Asn Gly Glu Trp Cys Glu Ala Gln Thr Lys Asn Gly Gln Gly Trp  
 195 200 205  
 Val Pro Ser Asn Tyr Ile Thr Pro Val Asn Ser Leu Glu Lys His Ser  
 210 215 220  
 Trp Tyr His Gly Pro Val Ser Arg Asn Ala Ala Glu Tyr Leu Leu Ser  
 225 230 235 240  
 Ser Gly Ile Asn Gly Ser Phe Leu Val Arg Glu Ser Glu Ser Ser Pro  
 245 250 255

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Gly Gln Arg Ser Ile Ser Leu Arg Tyr Glu Gly Arg Val Tyr His Tyr  
260 265 270

Arg Ile Asn Thr Ala Ser Asp Gly Lys Leu Tyr Val Ser Ser Glu Ser  
275 280 285

Arg Phe Asn Thr Leu Ala Glu Leu Val His His His Ser Thr Val Ala  
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Asp Gly Leu Ile Thr Thr Leu His Tyr Pro Ala Pro Lys Arg Asn Lys  
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Pro Thr Val Tyr Gly Val Ser Pro Asn Tyr Asp Lys  
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<212> DNA

<213> Homo sapiens

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cagcagaaga agtggtttcag aagctctccc ctgacatccg tggagctgca gatgctgacc 240  
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actaaagggtg aaaagctccg ggtcttaggc tataatcaca atggggaaatg gtgtgaagcc 600  
caaaccaaaa atggccaagg ctgggtccca agcaactaca tcacgccagt caacagctcg 660  
gagaacact cctggatcca tgggctctgt tcccgaatg ccgctgagta tctgctgagc 720  
agcgggataca atggcagctt ctgggtgcgt gagagtgaga gcagtcctgg ccaggagctc 780  
atctcgtga gatacgaagg gaggggtgtac cattacagga tcaactctgc ttctgatggc 840  
aagctctacg tctctccga gagccgcttc aacaccctgg ccgagtggtg tcatcatcat 900  
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<212> PRT

<213> Homo sapiens

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Ser Ile Pro Leu Thr Ile Asn Lys Glu His Asp Glu Ser Pro Gly Leu  
35 40 45

Tyr Gly Phe Leu Asn Val Ile Val His Ser Ala Thr Gly Phe Lys Gln  
50 55 60

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Ser Ser Asn Leu Tyr Cys Thr Leu Glu Val Asp Ser Phe Gly Tyr Phe  
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Val Asn Lys Ala Lys Thr Arg Val Tyr Arg Asp Thr Ala Glu Pro Asn  
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Leu Leu Ala Gly Pro  
100

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ggaacatgat gagctccgg ggctctatgg gtttctgaat gtcacgtgcc actcagccac 180  
tggtatttaag cagagttcaa atctgtactg caccctggag gtggattcct ttgggtattt 240  
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accca 305

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tggaccat 250

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<213> Homo sapiens

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cac 63

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Pro Pro Gly Tyr Gly

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20

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&lt;211&gt; 63

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 16

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ggc 63

&lt;210&gt; 17

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 17

Asp Gly Glu Gly Ala Phe His Gly Asp Ala Glu Ala Leu Gln Arg Pro  
1 5 10 15

Val Ala Ser Asp Phe

20

&lt;210&gt; 18

&lt;211&gt; 63

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 18

gatggcgagg gcgccttcca tggagacgca gaagcccttc agcggccagt agcatctgac 60  
ttt 63

&lt;210&gt; 19

&lt;211&gt; 140

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 19

Leu Leu Tyr Lys Pro Val Asp Arg Val Thr Arg Ser Thr Leu Val Leu  
1 5 10 15

His Asp Leu Leu Lys His Thr Pro Ala Ser His Pro Asp His Pro Leu  
20 25 30

Leu Gln Asp Ala Leu Arg Ile Ser Gln Asn Phe Leu Ser Ser Ile Asn  
35 40 45

Glu Glu Ile Thr Pro Arg Arg Gln Ser Met Thr Val Lys Lys Gly Glu  
50 55 60

Gly Glu Asp Arg Met Lys Ala Ser Ser Thr Arg Lys Arg Leu Leu Leu  
65 70 75 80

Met Glu Glu Ala Leu Gln Arg Pro Val Ala Ser Asp Phe Glu Pro Gln

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85

90

95

Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys Glu Asn Leu Leu Ala  
 100 105 110

Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val Ala Leu Tyr Asp Phe  
 115 120 125

Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr Lys  
 130 135 140

&lt;210&gt; 20

&lt;211&gt; 423

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 20

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 aag 423

&lt;210&gt; 21

&lt;211&gt; 307

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 21

Ala Asn Lys Gly Ser Lys Ala Thr Glu Arg Leu Lys Lys Lys Leu Ser  
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Glu Gln Glu Ser Leu Leu Leu Met Ser Pro Ser Met Ala Phe Arg  
 20 25 30

Val His Ser Arg Asn Gly Lys Ser Tyr Thr Phe Leu Ile Ser Ser Asp  
 35 40 45

Tyr Glu Arg Ala Glu Trp Arg Glu Asn Ile Arg Glu Gln Gln Lys Lys  
 50 55 60

Cys Phe Arg Ser Phe Ser Leu Thr Ser Val Glu Leu Gln Met Leu Thr  
 65 70 75 80

Asn Ser Cys Val Lys Leu Gln Thr Val His Ser Ile Pro Leu Thr Ile  
 85 90 95

Asn Lys Glu Glu Ala Leu Gln Arg Pro Val Ala Ser Asp Phe Glu Pro  
 100 105 110

Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys Glu Asn Leu Leu  
 115 120 125



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Ala Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val Ala Leu Tyr Asp  
 130 135 140

Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr Lys Gly Glu Lys  
 145 150 155 160

Leu Arg Val Leu Gly Tyr Asn His Asn Gly Glu Trp Cys Glu Ala Gln  
 165 170 175

Thr Lys Asn Gly Gln Gly Trp Val Pro Ser Asn Tyr Ile Thr Pro Val  
 180 185 190

Asn Ser Leu Glu Lys His Ser Trp Tyr His Gly Pro Val Ser Arg Asn  
 195 200 205

Ala Ala Glu Tyr Leu Leu Ser Ser Gly Ile Asn Gly Ser Phe Leu Val  
 210 215 220

Arg Glu Ser Glu Ser Ser Pro Gly Gln Arg Ser Ile Ser Leu Arg Tyr  
 225 230 235 240

Glu Gly Arg Val Tyr His Tyr Arg Ile Asn Thr Ala Ser Asp Gly Lys  
 245 250 255

Leu Tyr Val Ser Ser Glu Ser Arg Phe Asn Thr Leu Ala Glu Leu Val  
 260 265 270

His His His Ser Thr Val Ala Asp Gly Leu Ile Thr Thr Leu His Tyr  
 275 280 285

Pro Ala Pro Lys Arg Asn Lys Pro Thr Val Tyr Gly Val Ser Pro Asn  
 290 295 300

Tyr Asp Lys  
 305

&lt;210&gt; 22

&lt;211&gt; 922

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 22

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 tacacgtctc tgatctctcc tgactatgag cgtgcagagt ggaggaggaa catccgggag 180  
 cagcagaaga agtggtttcag aagcttctcc ctgacatccg tggagctgca gatgctgacc 240  
 aactcgtgtg tgaactccca gactgtccac agcattccgc tgaccatcaa taaggagaagaa 300  
 gcccttcacg gccccagtagc atctgacttt gagcctcagg gtctgagtga agccgctcgt 360  
 tggaaactcca aggaaaacct tctcgttgga cccagtga aa atgaccccaa ccttttcgtt 420  
 gcactgtatg attttgtggc cagtggagat aacactctaa gcataactaa aggtgaaaag 480  
 ctccgggtct taggctataa tcacaatggg gaatgggtgt aagcccaaac caaaaatggc 540  
 caaggctggg tcccaagcaa ctacatcacg ccagtcaca gtctggagaa acactcctgg 600  
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gtgtccccca actacgacaa gt

922

&lt;210&gt; 23

&lt;211&gt; 359

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 23

Tyr Gln Pro Tyr Gln Ser Ile Tyr Val Gly Gly Met Met Glu Gly Glu  
 1 5 10 15

Gly Lys Gly Pro Leu Leu Arg Ser Gln Ser Thr Ser Glu Gln Glu Lys  
 20 25 30

Arg Leu Thr Trp Pro Arg Arg Ser Tyr Ser Pro Arg Ser Phe Glu Asp  
 35 40 45

Cys Gly Gly Gly Tyr Thr Pro Asp Cys Ser Ser Asn Glu Asn Leu Thr  
 50 55 60

Ser Ser Glu Glu Asp Phe Ser Ser Gly Gln Ser Ser Arg Val Ser Pro  
 65 70 75 80

Ser Pro Thr Thr Tyr Arg Met Phe Arg Asp Lys Ser Arg Ser Pro Ser  
 85 90 95

Gln Asn Ser Gln Gln Ser Phe Asp Ser Ser Ser Pro Pro Thr Pro Gln  
 100 105 110

Cys His Lys Arg His Arg His Cys Pro Val Val Ser Glu Ala Thr  
 115 120 125

Ile Val Gly Val Arg Lys Thr Gly Gln Ile Trp Pro Asn Asp Gly Glu  
 130 135 140

Gly Ala Phe His Gly Asp Ala Glu Ala Leu Gln Arg Pro Val Ala Ser  
 145 150 155 160

Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala Arg Trp Asn Ser Lys  
 165 170 175

Glu Asn Leu Leu Ala Gly Pro Ser Glu Asn Asp Pro Asn Leu Phe Val  
 180 185 190

Ala Leu Tyr Asp Phe Val Ala Ser Gly Asp Asn Thr Leu Ser Ile Thr  
 195 200 205

Lys Gly Glu Lys Leu Arg Val Leu Gly Tyr Asn His Asn Gly Glu Trp  
 210 215 220

Cys Glu Ala Gln Thr Lys Asn Gly Gln Gly Trp Val Pro Ser Asn Tyr  
 225 230 235 240

Ile Thr Pro Val Asn Ser Leu Glu Lys His Ser Trp Tyr His Gly Pro  
 245 250 255

Val Ser Arg Asn Ala Ala Glu Tyr Leu Leu Ser Ser Gly Ile Asn Gly

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260 265 270

Ser Phe Leu Val Arg Glu Ser Glu Ser Ser Pro Gly Gln Arg Ser Ile  
275 280 285

Ser Leu Arg Tyr Glu Gly Arg Val Tyr His Tyr Arg Ile Asn Thr Ala  
290 295 300

Ser Asp Gly Lys Leu Tyr Val Ser Ser Glu Ser Arg Phe Asn Thr Leu  
305 310 315 320

Ala Glu Leu Val His His His Ser Thr Val Ala Asp Gly Leu Ile Thr  
325 330 335

Thr Leu His Tyr Pro Ala Pro Lys Arg Asn Lys Pro Thr Val Tyr Gly  
340 345 350

Val Ser Pro Asn Tyr Asp Lys  
355

<210> 24  
<211> 1079  
<212> DNA  
<213> Homo sapiens

<400> 24  
gtaccagccc taccagagca tctacgtcgg gggcatgatg gaagggagg gcaagggccc 60  
gtctctcgcc agccagagca cctctgagca ggaagaagcgc cttacctggc cccgcaggctc 120  
ctactccccc cggagttttg aggattgcgg agggcgctat acccggagct gcagctccaa 180  
tgagaacctc acctccagcg aggaggactt ctctctgggc cagtcacgac gcgtgtcccc 240  
aagcccccac acctaccgca tgttcgggga caaaagccgc tctccctcgc agaactcgca 300  
acagtccctc gacagcagca gtccccccac gccgcagtgc cataagcggc accggcactg 360  
cccggttggtc tgtgtccgagg ccaccatcgt gggcgctccgc aagaccgggc agatctggcc 420  
caacgatggc gagggcgctt tccatggaga cgcagaagcc cttcagcggc cagtagcatc 480  
tgactttgag cctcagggtc tgagtgaagc cgctcgtttg aactccaag aaaaccttct 540  
cgctgggccc agtgaaaatg accccaacct tttcgttgca ctgtatgatt ttgtggccag 600  
tggagataac actctaagca taactaaagg tgaagaagtc cgggtcttag gctataatca 660  
caatggggaa tggtgtgaag cccaaaccaa aaatggccaa ggctgggtcc caagcaacta 720  
catcacgcca gtcaacagtc tggagaaaca ctctcggtag catgggcctg tgtcccgcaa 780  
tgccgctgag tatctgctga gcagcgggat caatggcagc ttcttggtgc gtgagagtga 840  
gagcagtcct ggccagaggt ccatctcgct gagatacga gggagggtgt accattacag 900  
gatcaaacact gctctgatg gcaagctcta cgtctcctcc gagagccgct tcaacacctc 960  
ggccgagttg gttcatcatc attcaacggt ggccgacggg ctcatcacca cgctccatta 1020  
tccagcccca aagcgcaaca agcccactgt ctatggtgtg tcccccaact acgacaagt 1079

<210> 25  
<211> 34  
<212> PRT  
<213> Homo sapiens

<400> 25  
Val Gly Val Arg Lys Thr Gly Gln Ile Trp Pro Asn Asp Gly Glu Gly  
1 5 10 15  
Ala Phe His Gly Asp Ala Gly Lys Ser Pro Gly Leu Arg Leu Asn His  
20 25 30

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Asn Gly

&lt;210&gt; 26

&lt;211&gt; 106

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 26

tcgtagggcgt ccgcaagacc gggcagatct ggcccaacga tggcgagggc gcttccatg 60  
 gagacgcagg taaaagcccg ggtcttaggc taaatcaca tgggga 106

&lt;210&gt; 27

&lt;211&gt; 114

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 27

Met Ala Glu Cys Pro Thr Leu Gly Glu Ala Val Thr Asp His Pro Asp  
 1 5 10 15

Arg Leu Trp Ala Trp Glu Lys Phe Val Tyr Leu Asp Glu Lys Gln His  
 20 25 30

Ala Trp Leu Pro Leu Thr Ile Glu Ile Lys Asp Arg Leu Gln Leu Arg  
 35 40 45

Val Leu Leu Arg Arg Glu Asp Val Val Leu Gly Arg Pro Met Thr Pro  
 50 55 60

Thr Gln Ile Gly Pro Ser Leu Leu Pro Ile Met Trp Gln Leu Tyr Pro  
 65 70 75 80

Asp Gly Arg Tyr Arg Ser Ser Asp Ser Ser Phe Trp Arg Leu Val Tyr  
 85 90 95

His Ile Lys Ile Asp Gly Val Glu Asp Met Leu Leu Glu Leu Leu Pro  
 100 105 110

Asp Asp

&lt;210&gt; 28

&lt;211&gt; 1324

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 28

cttgagaggc tctggctctt gcttcttagg oggcccagg acgccatggc cgagtgcgcc 60  
 acactcgggg aggcagtcac cgaccacccg gaccgcctgt gggcctggga gaagtctgt 120  
 tatttggagc agaagcagca cgcctgggtg cccttaacca tcgagataaa ggaataggta 180  
 cagttacggc tgctcttgcc tcgggaagac gtgctcctgg ggaggcctat gaccccccacc 240  
 cagataggcc caagcctgct gcttatcatg tggcagctct accctgatgg acgataccga 300  
 tcttcagact ccagtttctg gcgcttagtg taccacatca agattgacgg cgtggaggac 360  
 atgctctctg agctgctgcc agatgactga tgtatggtct tggcagcacc tgtctccttt 420

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caccacaggg cctgagcctg gccagcctac aatggggatg ttgtgtttct gttcaccttc 480
gtttactatg cctgtgtctt ctccaccacg ctggggctct ggaggaatgg acagacagag 540
gatgagctct acccagggcc tgcaggacct gccgttagcc cactctgtct gcccttagcac 600
taccactcct gccaaaggag attccatttg gcagagcttc ttccagggtc ccagctatata 660
ctgctcctcg gcttttctca gctggatgat ggtcttcagc ctctttctgt cccttctgtc 720
ctccacagca ctagtatttc atgttgcaca cccactcagc tccgtgaact tgtgagaaca 780
cagccgatcc acctgagcag gacctctgaa accctggacc agtgggtcca catgggtgcta 840
gcctctcatg taaacacgcc tgcacaacgt gccctgccgt aaacacgcct gcaaacgctg 900
cctgcctgta aacacgcctg caaacgcctg ctgccacac aggtttcacg gcagctcaag 960
gaaaggcctg aaaggagccc ttatctgtgc tcaggactca gaagcctctg ggtcagtggt 1020
ccacatcccg ggaacgagca ggaaggccag ccggcgagcc ctgtggatga gccctcagaa 1080
cccttggtct gccacgtggg aaaaggagata gaggttggtt ttccccctt tatagatggt 1140
cacgcacctg ggtgttacaa agttgtatgt gccatgaata cttttgttaa tgattgatata 1200
aatgcaagat agtttatcta acttctgtgc caatcagctt ctatccttga cttagatctt 1260
ggtggagaga agtgagaata ggcagccccc aataaaaaaa tattcatgga aaaaaaaaaa 1320
aaaa

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<210> 29  
 <211> 114  
 <212> FRT  
 <213> Homo sapiens

<400> 29  
 Met Ala Glu Cys Pro Thr Leu Gly Glu Ala Val Thr Asp His Pro Asp  
 1 5 10 15  
 Arg Leu Trp Ala Trp Glu Lys Phe Val Tyr Leu Asp Glu Lys Gln His  
 20 25 30  
 Ala Trp Leu Pro Leu Thr Ile Glu Ile Lys Asp Arg Leu Gln Leu Arg  
 35 40 45  
 Val Leu Leu Arg Arg Glu Asp Val Val Leu Gly Arg Pro Met Thr Pro  
 50 55 60  
 Thr Gln Ile Gly Pro Ser Leu Leu Pro Ile Met Trp Gln Leu Tyr Pro  
 65 70 75 80  
 Asp Gly Arg Tyr Arg Ser Ser Asp Ser Ser Phe Trp Arg Leu Val Tyr  
 85 90 95  
 His Ile Lys Ile Asp Gly Val Glu Asp Met Leu Leu Glu Leu Leu Pro  
 100 105 110  
 Asp Asp

<210> 30  
 <211> 1324  
 <212> DNA  
 <213> Homo sapiens

<400> 30  
 cttgagaggg tctggctctt gcttcttagg cggcccgagg acgccatggc cgagtgcccg 60  
 acactcgggg aggcagtcac cgaccacccg gaccgctgt gggcctggga gaagtctgtg 120  
 tatttggagc agaagcagca cgcctggctg cccttaacca tcagatataa ggataggtta 180  
 cagttacggg tgctcttgcg tcgggaagac gtctgctctg ggaggcctat gacccccacc 240

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cagataggcc caagcctgct gcctatcatg tggcagctct accctgatgg acgataccga 300
tcctcagact ccagttctct gcgcttagtg taccacatca agattgacgg cgtggaggac 360
atgctctctg agctgctgcc agatgactga tgtatggtct tggcagcacc tgtctccttt 420
caccocaggg cctgagcctg gccagcctac aatggggatg tctgtttctt gttcaccttc 480
gtttactatg cctgtgtctt ctccaccacg ctgggggtctg ggaggaatgg acagacagag 540
gatgagctct acccaggggc tgcaggacct gcctgtagcc cactctgtct gccttagcac 600
taccactcct gccaaaggag attccatttg gcagagcttc ttccagggtg ccagctatac 660
ctgtgctctg gcttttctca gctggatgat ggtcttcagc ctctttctgt cctctctgtc 720
cctcacagca ctagtatttc atgttgacaa cccactcagc tctgtgaact tgtgagaaca 780
cagcgcgatt accctgagcag gacctctgaa accctggacc agtggctctc catgggtgct 840
cctgtgcgatg taacacgcgc tgcacacgct gcctgcgggt aaacacgcct gcaaacgcgt 900
cgctgccgta aacacgcctg caaacgctgc ctgccacac aggttcacgt gcagctcaag 960
gaaaggcctg aaaggagccc ttatctgtgc tcaggactca gaagcctctg ggtcagtggt 1020
ccacatcccg ggacgcagca ggaggccagg ccggcgagcc ctgtggatga gccctcagaa 1080
cccttggctt gccacgtggt aaaagggata gaggttgggt ttccccctt tatagatggt 1140
cacgcacctg ggtgttaca agttgtatgt ggcataata cttttgttaa tgattgatta 1200
aatgcaagat agtttatcta acttcgtgag caatcagctt ctatccttga cttagattct 1260
ggtggagaga agtgagaata ggcagccccc aaataaaaaa tattcatgga aaaaaaaaaa 1320
aaaa 1324

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<210> 31  
 <211> 560  
 <212> DNA  
 <213> Homo sapiens

```

<400> 31
gtcgactgtg agtcccagc agaggcccag agtcccgtc cggcagccga ggaagcggg 60
ggggtcttcc agaagaagaa agggccaagg tcaccccggt gcctctccag cagcagcaga 120
gggcggcggg cgggtgtcgt gctggccggg gcctcgagga aggcgcgggc cagctggggc 180
cgggtctctg ttcccaggag ctgccaccgt tccaggagac aagtcaggcc gggacgcttag 240
cgctgcgcgc ggaccctcac ttgccaccaaa ggaccccaaa aaccccgccc catccttagc 300
gcctgcgcgg gccctcact tgcaccaaag acccccacaa accccgccc atcctgcctt 360
acgccccgcc caaaggctgt tctcccgacc cggggtcccg ccccaagacc gtctctccgc 420
cccgcgcgtt ggtggcgccc gcctgctgcc cggatataaa gggctcgccc cacatcccg 480
ggaccagcga gcggccttga gaggtctctg ctctgtctc taggcggccc caggcagccc 540
atggccgagt gcccgacact

```

<210> 32  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

```

<400> 32
Phe Ala Gly Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Gly
  1           5           10           15

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
      20           25           30

Phe Thr Phe Ser Ser Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly
      35           40           45

Lys Gly Leu Val Trp Val Ser Arg Ile Asn Ser Asp Gly Ser Ser Thr
      50           55           60

Ser Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn

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65		70		75		80
Ala Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp						
	85			90		95
Thr Ala Val Tyr Tyr Cys Ala Arg Asp Pro Thr Gly Gly Ser Tyr Ile						
	100		105		110	
Pro Thr Phe Gly Arg Gly Thr Ser Leu Ile Val His Pro						
	115		120		125	

<210> 33  
 <211> 375  
 <212> DNA  
 <213> Homo sapiens

<400> 33  
 tttgcagggtg tccagtgtga ggtgcagctg gtggagtcog ggggaggctt agttcagcct 60  
 ggggggtccc tgagactctc ctgtgcagcc tctggattca ccttcagtag ctactggatg 120  
 cactgggtcc gccaaagctcc aggggaagggg ctgggtgtggg tctcacgtat taatagtgat 180  
 gggagtagca caagctacgc ggactcogtg aagggccgat tcaccatctc cagagacaac 240  
 gccagaaca cgtgtatct gcaaatgaac agtctgagag cogaggacac ggctgtgtat 300  
 tactgtgcaa gagatccaac aggaggaagc tacataccta catttgggaag aggaaccagc 360  
 cttattgttc atccg 375

<210> 34  
 <211> 125  
 <212> FRT  
 <213> Homo sapiens

<400> 34  
 Thr Gly Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu  
 1 5 10 15  
 Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr  
 20 25 30  
 Ser Ile Ser Ser Gly Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly  
 35 40 45  
 Lys Gly Leu Glu Trp Ile Gly Ser Ile Tyr His Ser Gly Ser Thr Tyr  
 50 55 60  
 Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser  
 65 70 75 80  
 Lys Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr  
 85 90 95  
 Ala Val Tyr Tyr Cys Ala Arg Val Arg Arg Arg Tyr Ser Ser Ala Ser  
 100 105 110  
 Lys Ile Ile Phe Gly Ser Gly Thr Arg Leu Ser Ile Arg  
 115 120 125

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<210> 35  
 <211> 377  
 <212> DNA  
 <213> Homo sapiens

<400> 35  
 tcacaggggt cctgtccag gtgcagctgc aggagtcggg ccacaggactg gtgaagcctt 60  
 cggagaccct gtccctcacc tgcactgtct ctgggtactc catcagcagt gggtactact 120  
 ggggtggat ccggcagccc ccagggaagg ggctggagtg gattgggagt atctatcata 180  
 gtggggagcac ctactacaac ccgtccctca agagtcgagt caccatatca gtacacacgt 240  
 ccaagaacca gttctccctg aagctgagct ctgtgaccgc cgcagacacg gccgtgtatt 300  
 actgtgcgag agtcgcgcgg aggtacagca gtgcttccaa gataatcttt ggatcaggga 360  
 ccagactcag catccgg 377

<210> 36  
 <211> 140  
 <212> PRT  
 <213> Homo sapiens

<400> 36  
 Met Lys His Leu Trp Phe Phe Leu Leu Val Ala Ala Pro Arg Trp  
 1 5 10 15  
 Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys  
 20 25 30  
 Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile  
 35 40 45  
 Ser Ser Gly Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly  
 50 55 60  
 Leu Glu Trp Ile Gly Ser Ile Tyr His Ser Gly Ser Thr Tyr Tyr Asn  
 65 70 75 80  
 Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn  
 85 90 95  
 Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val  
 100 105 110  
 Tyr Tyr Cys Ala Arg Val Arg Arg Arg Tyr Ser Ser Ala Ser Lys Ile  
 115 120 125  
 Ile Phe Gly Ser Gly Thr Arg Leu Ser Ile Arg Pro  
 130 135 140

<210> 37  
 <211> 675  
 <212> DNA  
 <213> Homo sapiens

<400> 37  
 ccacccacat gcaaatcctc acttaggcgc ccacaggaag ccacaacaca ttctcttaaa 60  
 ttcaggtcca actcataagg gaaatgcttt ctgagagtcga tggacctctc gtgcaagaac 120  
 atgaagcacc tgtgggtttt cctcctgctg gtggcagctc ccagatgtga gtgtctcagg 180



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gatccagaag tgaagatatg ggaagtgcct ctgatccag ggctcaccgt ggggtttttct 240
gttcacagggt gtctctgtccc aggtgcagct gcaggagtcg ggcccaggagc tgggtgaagcc 300
ttcggagagac ctgtccctca cctgcactgt ctctgggttac tccatcagca gtggttacta 360
ctggggctgag atcoggcagc ccccaggga ggggctggag tggattggga gtatctatca 420
tagtgggagc acctactaca acccgctccct caagagtoga gtcaccatat cagtagacac 480
gtccaagaac cagttctccc tgaagctgag ctctgtgacc gccgcagaca cgcccggtga 540
ttactgtggg agagtcogtc ggaggtacag cagtgtcttc aagataatct ttggatcagg 600
gaccagactc agcatccggc caagtaagta gaatgaagca ggagagcaag ggaggacgga 660
caactatttc ttctt 675

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<210> 38  
 <211> 158  
 <212> FRT  
 <213> Homo sapiens

```

<400> 38
Met Val Thr Gly Gly Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly
  1           5           10          15
Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val
  20           25           30
Ser Gly Tyr Ser Ile Ser Ser Gly Tyr Tyr Trp Gly Trp Ile Arg Gln
  35           40           45
Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Ser Ile Tyr His Ser Gly
  50           55           60
Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val
  65           70           75           80
Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala
  85           90           95
Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Val Arg Arg Arg Tyr Ser
  100          105          110
Ser Ala Ser Lys Ile Ile Phe Gly Ser Gly Thr Arg Leu Ser Ile Arg
  115          120          125
Pro Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln Leu Arg Asp Ser
  130          135          140
Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp Phe Asp
  145          150          155

```

<210> 39  
 <211> 508  
 <212> DNA  
 <213> Homo sapiens

```

<400> 39
tgtctctcta aaactcggga atttgtcact gaaatgggtga caggagggggt cctgtcccag 60
gtgcagctgc aggtgcggg cccaggactg gtgaagcctt cggagaccct gtcctcacc 120
tgcactgtct ctggttactc catcagcagt ggttactact ggggctggat ccggcagccc 180
ccagggaagg ggctggagtg gattgggagt atctatcata gtgggagcac ctactacaac 240

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ccgtccctca agagtcgagt caccatatca gtagacacgt ccaagaacca gttctccctg 300
aagctgagct ctgtgacgcg cgcagacacg gccgtgtatt actgtgcgag agtcgcgtcg 360
aggtacagca gtgcttccaa gataatcttt ggatcaggga ccagactcag catccggcca 420
aataccaga accctgaccc tgccgtgtac cagctgagag actctaaatc cagtgacaag 480
tctgtctgcc tattcacaga ttttgatt
508

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&lt;210&gt; 40

&lt;211&gt; 162

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 40

```

Met Ala Glu Ala Leu His Gly Lys Arg Val Leu Ser Gln Val Gln Leu
1 5 10 15
Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu
20 25 30
Ala Cys Thr Val Ser Gly Tyr Ser Ile Ser Ser Gly Tyr Trp Trp Gly
35 40 45
Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Ser Ile
50 55 60
Tyr His Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser Arg Val
65 70 75 80
Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys Leu Ser
85 90 95
Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Val Arg
100 105 110
Arg Arg Tyr Ser Ser Ala Ser Lys Ile Ile Phe Gly Ser Gly Thr Arg
115 120 125
Leu Ser Ile Arg Pro Asn Ile Gln Asn Pro Asp Pro Ala Val Tyr Gln
130 135 140
Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu Phe Thr Asp
145 150 155 160
Phe Asp

```

&lt;210&gt; 41

&lt;211&gt; 616

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 41

```

tgtcctctga aaactcggga atttgtcact gaaatggtga caggagccta cagggtggcag 50
atggaaccta tcaacacagt tgtgttagaa gaaggatttc ctagagagac cctgactcaa 120
tgatgatata tggctgaagc attgcatgga aaacgggtcc tgtcccaggt gcagctgcag 180
gagtcggggcc caggactggt gaagccttcg gagaccctgt cctcgcctg cactgtctct 240
ggttactcca tcagcagtggt ttactactgg ggctggatcc ggcagcccc aggggaaggg 300
ctggagtgga ttgggagtat ctatcatagt gggagcacct actacaaccc gtcctccaag 360

```

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agtgcagtcacccatcatcagtagacacgtccagaaccagttctccctgaa gctgagctct 420
gtgaccgcgcagacacggccgtgtattactgtgcgagagtcctgcggaggtacacagcag 480
gcttccaaga taatctttggatcaggagaccagactcagca tccggccaaa tatccagaac 540
cctgaccctgcctgtgtacca gctgagagactctaaatcca gtgacaagtc tgbtctgccta 600
ttcaccgatt ttgatt 616

```

&lt;210&gt; 42

&lt;211&gt; 550

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 42

```

Gly Tyr Gln Leu His Gly Ala Glu Val Asn Gly Gly Leu Pro Ser Ala
 1             5             10             15

Ser Ser Phe Ser Ser Ala Pro Gly Ala Thr Tyr Gly Val Ser Ser His
 20             25             30

Thr Pro Pro Val Ser Gly Ala Asp Ser Leu Leu Gly Ser Arg Gly Thr
 35             40             45

Thr Ala Gly Ser Ser Gly Asp Ala Leu Gly Lys Ala Leu Ala Ser Ile
 50             55             60

Tyr Ser Pro Asp His Ser Ser Asn Asn Phe Ser Ser Ser Pro Ser Thr
 65             70             75             80

Pro Val Gly Ser Pro Gln Gly Leu Ala Gly Thr Ser Gln Trp Pro Arg
 85             90             95

Ala Gly Ala Pro Gly Ala Leu Ser Pro Ser Tyr Asp Gly Gly Leu His
100             105             110

Gly Leu Gln Ser Lys Ile Glu Asp His Leu Asp Glu Ala Ile His Val
115             120             125

Leu Arg Ser His Ala Val Gly Thr Ala Gly Asp Met His Thr Leu Leu
130             135             140

Pro Gly His Gly Ala Leu Ala Ser Gly Phe Thr Gly Pro Met Ser Leu
145             150             155             160

Gly Gly Arg His Ala Gly Leu Val Gly Gly Ser His Pro Glu Asp Gly
165             170             175

Leu Ala Gly Ser Thr Ser Leu Met His Asn His Ala Ala Leu Pro Ser
180             185             190

Gln Pro Gly Thr Leu Pro Asp Leu Ser Arg Pro Pro Asp Ser Tyr Ser
195             200             205

Val Leu Ser Ile Arg Gly Ala Gln Glu Glu Glu Pro Thr Asp Pro Gln
210             215             220

Leu Met Arg Leu Asp Asn Met Leu Leu Ala Glu Gly Val Ala Gly Pro
225             230             235             240

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Glu Lys Gly Gly Gly Ser Ala Ala Ala Ala Ala Ala Ala Ser  
                             245                            250                            255

Gly Gly Ala Gly Ser Asp Asn Ser Val Glu His Ser Asp Tyr Arg Ala  
                             260                            265                            270

Lys Leu Ser Gln Ile Arg Gln Ile Tyr His Thr Glu Leu Glu Lys Tyr  
                             275                            280                            285

Glu Gln Ala Cys Asn Glu Phe Thr Thr His Val Met Asn Leu Leu Arg  
                             290                            295                            300

Glu Gln Ser Arg Thr Arg Pro Ile Ser Pro Lys Glu Ile Glu Arg Met  
                             305                            310                            315                            320

Val Ser Ile Ile His Arg Lys Phe Ser Ser Ile Gln Met Gln Leu Lys  
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Gln Ser Thr Cys Glu Ala Val Met Ile Leu Arg Ser Arg Phe Leu Asp  
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Asn Glu Tyr Phe Tyr Ser His Leu Ser Asn Pro Tyr Pro Ser Glu Glu  
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Ala Lys Glu Glu Leu Ala Lys Lys Cys Gly Ile Thr Val Ser Gln Val  
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Ser Asn Trp Phe Gly Asn Lys Arg Ile Arg Tyr Lys Lys Asn Ile Gly  
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Lys Phe Gln Glu Glu Ala Asn Ile Tyr Ala Ala Lys Thr Ala Val Thr  
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Ala Thr Asn Val Ser Ala His Gly Ser Gln Ala Asn Ser Pro Ser Thr  
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Pro Asn Ser Ala Gly Ser Ser Ser Phe Asn Met Ser Asn Ser Gly  
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Asp Leu Phe Met Ser Val Gln Ser Leu Asn Gly Asp Ser Tyr Gln Gly  
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Ala Gln Val Gly Ala Asn Val Gln Ser Gln Val Asp Thr Leu Arg His  
                             485                            490                            495

Val Ile Ser Gln Thr Gly Gly Tyr Ser Asp Gly Leu Ala Ala Ser Gln  
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Met Tyr Ser Pro Gln Gly Ile Ser Ala Asn Gly Gly Trp Gln Asp Ala  
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His Ser Asp Thr Ser Asn

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545

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Gly Lys Gly Arg Pro Ala Ser Leu Ala Gly Ala Gln Phe Gly Gly Ser  
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                   20                                  25                                  30  
 Pro Pro Leu Pro Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys  
           35                                  40                                  45  
 Ser Ser Gly Tyr His Tyr Gly Val Ser Ala Cys Glu Gly Cys Lys Gly  
           50                                  55                                  60  
 Phe Phe Arg Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg  
           65                                  70                                  75                                  80  
 Asp Lys Asn Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr  
                   85                                  90                                  95  
 Cys Arg Leu Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ser Val  
                   100                                  105                                  110  
 Arg Asn Asp Arg Asn Lys Lys Lys Lys Glu Val Pro Lys Pro Glu Cys  
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 Ser Glu Ser Tyr Thr Leu Thr Pro Glu Val Gly Glu Leu Ile Glu Lys  
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 Val Arg Lys Ala His Gln Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly  
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 Lys Tyr Thr Thr Asn Asn Ser Ser Glu Gln Arg Val Ser Leu Asp Ile  
                   165                                  170                                  175  
 Asp Leu Trp Asp Lys Phe Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys  
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 Thr Val Glu Phe Ala Lys Gln Leu Pro Gly Phe Thr Thr Leu Thr Ile  
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 Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys Leu Asp Ile Leu Ile  
           210                                  215                                  220

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Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln Asp Thr Met Thr Phe  
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Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met His Asn Ala Gly Phe  
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Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala Asn Gln Leu Leu Pro  
260 265 270

Leu Glu Met Asp Asp Ala Glu Thr Gly Leu Leu Ser Ala Ile Cys Leu  
275 280 285

Ile Cys Gly Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met  
290 295 300

Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Val Tyr Val Arg Lys Arg  
305 310 315 320

Arg Pro Ser Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr  
325 330 335

Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu  
340 345 350

Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu  
355 360 365

Glu Asn Ser Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly  
370 375 380

Gly Arg Asp Gly Gly Gly Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro  
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Ser Leu Ser Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro  
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&lt;210&gt; 47

&lt;211&gt; 1284

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

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&lt;210&gt; 48

&lt;211&gt; 797

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 48

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Arg Pro Gln Glu Pro Thr Met Pro Pro Pro Glu Thr Pro Ser Glu Gly
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Arg Gln Pro Ser Pro Ser Pro Ser Pro Thr Glu Arg Ala Pro Ala Ser
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Glu Glu Glu Phe Gln Phe Leu Arg Cys Gln Gln Cys Gln Ala Glu Ala
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Lys Cys Pro Lys Leu Leu Pro Cys Leu His Thr Leu Cys Ser Gly Cys
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Leu Glu Ala Ser Gly Met Gln Cys Pro Ile Cys Gln Ala Pro Trp Pro
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Leu Gly Ala Asp Thr Pro Ala Leu Asp Asn Val Phe Phe Glu Ser Leu
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Gln Arg Arg Leu Ser Val Tyr Arg Gln Ile Val Asp Ala Gln Ala Val
        115           120           125

Cys Thr Arg Cys Lys Glu Ser Ala Asp Phe Trp Cys Phe Glu Cys Glu
        130           135           140

Gln Leu Leu Cys Ala Lys Cys Phe Glu Ala His Gln Trp Phe Leu Lys
        145           150           155           160

His Glu Ala Arg Pro Leu Ala Glu Leu Arg Asn Gln Ser Val Arg Glu
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Phe Leu Asp Gly Thr Arg Lys Thr Asn Asn Ile Phe Cys Ser Asn Pro
        180           185           190

Asn His Arg Thr Pro Thr Leu Thr Ser Ile Tyr Cys Arg Gly Cys Ser
        195           200           205

Lys Pro Leu Cys Cys Ser Cys Ala Leu Leu Asp Ser Ser His Ser Glu
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 His Val Arg Ala Gln Glu Arg Glu Leu Leu Glu Ala Val Asp Ala Arg  
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 Tyr Gln Arg Asp Tyr Glu Glu Met Ala Ser Arg Leu Gly Arg Leu Asp  
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 Pro Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys Ser Ser Gly  
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 Tyr His Tyr Gly Val Ser Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg  
 435 440 445  
 Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg Asp Lys Asn  
 450 455 460  
 Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr Cys Arg Leu  
 465 470 475 480  
 Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ser Val Arg Asn Asp  
 485 490 495  
 Arg Asn Lys Lys Lys Lys Glu Val Pro Lys Pro Glu Cys Ser Glu Ser  
 500 505 510  
 Tyr Thr Leu Thr Pro Glu Val Gly Glu Leu Ile Glu Lys Val Arg Lys  
 515 520 525  
 Ala His Gln Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly Lys Tyr Thr

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530	535	540
Thr Asn Asn Ser Ser Glu Gln Arg Val Ser Leu Asp Ile Asp Leu Trp		
545	550	555
Asp Lys Phe Ser Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys Thr Val Glu		
	565	570
Phe Ala Lys Gln Leu Pro Gly Phe Thr Thr Leu Thr Ile Ala Asp Gln		
	580	585
Ile Thr Leu Leu Lys Ala Ala Cys Leu Asp Ile Leu Ile Leu Arg Ile		
	595	600
Cys Thr Arg Tyr Thr Pro Glu Gln Asp Thr Met Thr Phe Ser Asp Gly		
	610	615
Leu Thr Leu Asn Arg Thr Gln Met His Asn Ala Gly Phe Gly Pro Leu		
625	630	635
Thr Asp Leu Val Phe Ala Phe Ala Asn Gln Leu Leu Pro Leu Glu Met		
	645	650
Asp Asp Ala Glu Thr Gly Leu Leu Ser Ala Ile Cys Leu Ile Cys Gly		
	660	665
Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met Leu Gln Glu		
	675	680
Pro Leu Leu Glu Ala Leu Lys Val Tyr Val Arg Lys Arg Arg Pro Ser		
	690	695
Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr Asp Leu Arg		
705	710	715
Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu Lys Met Glu		
	725	730
Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu Glu Asn Ser		
	740	745
Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly Arg Asp		
	755	760
Gly Gly Gly Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro Ser Leu Ser		
	770	775
Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro		
785	790	795

&lt;210&gt; 49

&lt;211&gt; 3036

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 49

ctcccccttca gcttctcttc acgcactcca agatctaaac cgagaatcga aactaagctg 50

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gggtccatgg	agcctgcacc	cgcccgatct	cgcaggcccc	agcaggagccc	cgcccggccc	120
caggagccca	ccatgcctcc	ccccgagacc	ccctctgaag	gccgcagccc	cagcccccage	180
cccagcccta	cagagcgagc	ccccgcttcg	gaggaggaggt	tccagtttct	gcgctgccag	240
caatgcgcagg	cggagagccaa	gtgcgccgaag	ctgctgcctt	gtctgcacac	gctgtgtcca	300
gagtgctctgg	aggcgctcggg	catgcagctgc	cccatctgcc	aggcgccctg	gccccctagg	360
gcagacacac	ccgcctctgga	taacgtcttt	ttcgagagtc	tgcagcggcg	cctgtcgggt	420
taccgcgcaga	ttgtgctatgc	gcaggctctgt	tgaccacctg	gcaaaagagtc	ggccgacttc	480
tggtgtcttgg	atgtgcgagca	gctcctctgc	gccaaagtgt	tgcaggccaca	ccagtggctc	540
ctcaagcacgc	aggccccggcc	cctagcagag	ctgcgcacac	agtccgttgcg	tgagttctctg	600
gacggcgaccc	gcgaagaccaa	caacatcttc	tgctcccaacc	ccaaccaccg	cacccctacg	660
ctcaggccaga	tctactgtccg	aggatgttcc	aagccgctgt	gctgtctctg	cgccctcctt	720
gacagcagcc	acagtgtagct	caagtgcgac	atcagcgcag	agatccagca	gcgacaggag	780
gagctggagc	ccatgacgca	ggcgctgcag	gagcaggata	gtgccttttg	cgcgggttcc	840
gcgcagatgc	agccggccgt	cggccagctg	ggccgcgcgc	gtgcgcagac	cgaggagctg	900
atccgcgcgc	gcgtgcgcga	ggtggtagct	cacgtgcggg	ctcaggagcg	cgagctgctg	960
gaggctgtgg	acgcgcggta	ccagcgcgac	tacaggagga	tgcccaagtgc	tggggtccgc	1020
cttgatgctg	tctgcagcgc	catccgcagc	ggcagcgcgc	tggtgcagag	gatgaaagct	1080
tacgcctcgg	accaggagggt	gctggacatg	cacggtttcc	tgccgcagac	gctctgcgc	1140
ctgcgcgcag	aggagcccca	gagcctgcaa	gctgcgcgtg	gcaccgatgc	ccttcgagac	1200
ttcaaggttg	gcctgcaggga	cctcagctct	tgcatcaccc	agggggaagc	catctgagacc	1260
cagaagcaga	gttctgaaga	gatagtcccc	agccctccct	cgccaccccc	tctacccccc	1320
atctacaagc	cttgcctttgt	ctgtcaggac	aagtccctcag	gctaccacta	tggggctcagc	1380
gcctgtgagg	gtgcgaaggg	cttcttccgc	cgcagcatcc	agaagaacat	gggtgcacag	1440
tgctaccggg	acaagaactg	catcatcaac	aaggtgaccc	ggaaccgctg	ccagtactgc	1500
cgactgcaga	agtgtcttga	agtgggcatg	tccaaggagt	ctgtgagaaa	cgaccgaaac	1560
aagaagaaga	aggaggtgcc	caagcccgag	tgctctgaga	gctacacgct	gacgcgggag	1620
gtggggggagc	tcaattgagaa	ggcgccgcaa	gcgcaccagg	aaacctctcc	tgccctctgc	1680
cagctggggca	aatacactac	gaacaacacg	tcagaacaac	gtgtctctct	ggacattgac	1740
ctcttgggaca	agttcaagtga	actctccacc	aagtgcacat	ttaagactgt	ggagttcgcc	1800
gaagcagctgc	ccggcttcaac	cacctccacc	atcgccgacc	agatcacccct	cctcaaggct	1860
cctgcctctg	acatcctgat	cctgcggatc	tgcaacgggt	acacgcccca	gcagagacac	1920
atgacctctc	cggacgggct	gaccttgaa	cggaccocaga	tgcaacaacc	tggtctcggc	1980
ccccctaccg	acctggctct	tgccctcgcc	aaccagctgc	tgcccctgga	gatggatgat	2040
gcggagacgg	ggctgtctcag	cgccatctgc	ctcatctgcg	gagaccgcga	ggacctggag	2100
cagccgggac	gggtggacat	gctgcaggag	ccgctgctgg	aggcgctaaa	ggtctacgtg	2160
cgggaagcga	ggccacgcg	ccccacatg	ttccccaaga	tgctaatgaa	gattactgac	2220
ctgcgaagca	tcagccgcga	gggggctgag	cggggtgatca	cgtggaagat	ggagatcccc	2280
ggctccatgc	cgcctctcat	ccaggaaatg	ttggagaact	cagagggcct	ggacactctg	2340
agcggagcag	cggggggggtg	ggggcgggag	gggggtggcc	tgcccctccc	gccagggcagc	2400
tgtagcccca	gctccagccc	cagctccaac	agaagcagcc	cggccaccca	ctccccgtga	2460
ccgcccacgc	caatggagca	cagccctcgc	cctccgcccc	ggctttttct	tgcttttcta	2520
cgacacatgt	gaccccgcac	cagccctgcc	cccacctgcc	ctcccgggga	gtactgggga	2580
ccttccctgg	gggacggggga	gggagggagc	agcgactcct	tggaacagag	cctggggcct	2640
cagtggaact	cctgtcccca	cagcctgggc	tgactgcaga	ggccgagggc	aggaactgag	2700
tgagggccct	ggctcctgggt	ctcaggatgg	gtcctggggg	cctcgtgttc	atacaagcac	2760
ccctctgcccc	agctccaccac	atcttcatca	ccagcaaacg	ccaggactgt	gctcccccat	2820
cctcagaact	cacaagccat	tgctccccag	ctggggaacc	tcaacctccc	cctgcctctg	2880
gttggtagca	gaggggggtgc	gacagggggc	gggggttccc	cctgtacata	ccctgcacata	2940
ccaaccccag	gtatttaattc	tcgctgggtt	tggttttatt	ttaatttttt	tggttttgatt	3000
tttttaataa	gaattttcat	tttaagcaaa	aaaaaa			3036

&lt;210&gt; 50

&lt;211&gt; 99

&lt;212&gt; FRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 50

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Asp Val Ser Asn Thr Thr Thr Ala Gln Lys Arg Lys Cys Ser Gln Thr  
 1 5 10 15  
 Gln Cys Pro Arg Lys Val Ile Lys Met Glu Ser Glu Glu Gly Lys Glu  
 20 25 30  
 Ala Arg Leu Ala Leu Pro Ala Pro Gly Pro Tyr Ser Thr Pro Leu Arg  
 35 40 45  
 Thr Pro Leu Trp Asn Gly Ser Asn His Ser Ile Glu Thr Gln Ser Ser  
 50 55 60  
 Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro Pro Pro Leu Pro  
 65 70 75 80  
 Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys Ser Ser Gly Tyr  
 85 90 95  
 His Tyr Gly

<210> 51  
 <211> 296  
 <212> DNA  
 <213> Homo sapiens

<400> 51  
 gatgtctcca atacaacgac agcccagaag aggaagtgc gccagaccca gtgccccagg 60  
 aaggtcatca agatggagtc tgaggagggg aaggaggcaa ggttgctct cccgccccg 120  
 ggctcgact ccacccgct ccggactcgg cttgggaat gctcaaacca ctccattgg 180  
 acccagagca gcagttctga agagatagt cccagccctc cctgcacc cctctacc 240  
 cgcattcata agccttgctt tgtctgtcag gacaagtct caggctacca ctatgg 296

<210> 52  
 <211> 858  
 <212> PRT  
 <213> Homo sapiens

<400> 52  
 Met Asp Leu Thr Lys Met Gly Met Ile Gln Leu Gln Asn Pro Ser His  
 1 5 10 15  
 Pro Thr Gly Leu Leu Cys Lys Ala Asn Gln Met Arg Leu Ala Gly Thr  
 20 25 30  
 Leu Cys Asp Val Val Ile Met Val Asp Ser Gln Glu Phe His Ala His  
 35 40 45  
 Arg Thr Val Leu Ala Cys Thr Ser Lys Met Phe Glu Ile Leu Phe His  
 50 55 60  
 Arg Asn Ser Gln His Tyr Thr Leu Asp Phe Leu Ser Pro Lys Thr Phe  
 65 70 75 80  
 Gln Gln Ile Leu Glu Tyr Ala Tyr Thr Ala Thr Leu Gln Ala Lys Ala  
 85 90 95

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Glu Asp Leu Asp Asp Leu Leu Tyr Ala Ala Glu Ile Leu Glu Ile Glu  
 100 105 110  
 Tyr Leu Glu Glu Gln Cys Leu Lys Met Leu Glu Thr Ile Gln Ala Ser  
 115 120 125  
 Asp Asp Asn Asp Thr Glu Ala Thr Met Ala Asp Gly Gly Ala Glu Glu  
 130 135 140  
 Glu Glu Asp Arg Lys Ala Arg Tyr Leu Lys Asn Ile Phe Ile Ser Lys  
 145 150 155 160  
 His Ser Ser Glu Glu Ser Gly Tyr Ala Ser Val Ala Gly Gln Ser Leu  
 165 170 175  
 Pro Gly Pro Met Val Asp Gln Ser Pro Ser Val Ser Thr Ser Phe Gly  
 180 185 190  
 Leu Ser Ala Met Ser Pro Thr Lys Ala Ala Val Asp Ser Leu Met Thr  
 195 200 205  
 Ile Gly Gln Ser Leu Leu Gln Gly Thr Leu Gln Pro Pro Ala Gly Pro  
 210 215 220  
 Glu Glu Pro Thr Leu Ala Gly Gly Gly Arg His Pro Gly Val Ala Glu  
 225 230 235 240  
 Val Lys Thr Glu Met Met Gln Val Asp Glu Val Pro Ser Gln Asp Ser  
 245 250 255  
 Pro Gly Ala Ala Glu Ser Ser Ile Ser Asp Gly Met Gly Asp Lys Val  
 260 265 270  
 Glu Glu Arg Gly Lys Glu Gly Pro Gly Thr Pro Thr Arg Ser Ser Val  
 275 280 285  
 Ile Thr Ser Ala Arg Glu Leu His Tyr Gly Arg Glu Glu Ser Ala Glu  
 290 295 300  
 Gln Val Pro Pro Pro Ala Glu Ala Gly Gln Ala Pro Thr Gly Arg Pro  
 305 310 315 320  
 Glu His Pro Ala Pro Pro Pro Glu Lys His Leu Gly Ile Tyr Ser Val  
 325 330 335  
 Leu Pro Asn His Lys Ala Asp Ala Val Leu Ser Met Pro Ser Ser Val  
 340 345 350  
 Thr Ser Gly Leu His Val Gln Pro Ala Leu Ala Val Ser Met Asp Phe  
 355 360 365  
 Ser Thr Tyr Gly Gly Leu Leu Pro Gln Gly Phe Ile Gln Arg Glu Leu  
 370 375 380  
 Phe Ser Lys Leu Gly Glu Leu Ala Val Gly Met Lys Ser Glu Ser Arg  
 385 390 395 400  
 Thr Ile Gly Glu Gln Cys Ser Val Cys Gly Val Glu Leu Pro Asp Asn



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405	410	415
Glu Ala Val Glu Gln His Arg Lys Leu His Ser Gly Met Lys Thr Tyr		
420	425	430
Gly Cys Glu Leu Cys Gly Lys Arg Phe Leu Asp Ser Leu Arg Leu Arg		
435	440	445
Met His Leu Leu Ala His Ser Ala Ile Glu Thr Gln Ser Ser Ser Ser		
450	455	460
Glu Glu Ile Val Pro Ser Pro Pro Ser Pro Pro Pro Leu Pro Arg Ile		
465	470	475
Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys Ser Ser Gly Tyr His Tyr		
485	490	495
Gly Val Ser Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Ser Ile		
500	505	510
Gln Lys Asn Met Val Tyr Thr Cys His Arg Asp Lys Asn Cys Ile Ile		
515	520	525
Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr Cys Arg Leu Gln Lys Cys		
530	535	540
Phe Glu Val Gly Met Ser Lys Glu Ser Val Arg Asn Asp Arg Asn Lys		
545	550	555
Lys Lys Lys Glu Val Pro Lys Pro Glu Cys Ser Glu Ser Tyr Thr Leu		
565	570	575
Thr Pro Glu Val Gly Glu Leu Ile Glu Lys Val Arg Lys Ala His Gln		
580	585	590
Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly Lys Tyr Thr Thr Asn Asn		
595	600	605
Ser Ser Glu Gln Arg Val Ser Leu Asp Ile Asp Leu Trp Asp Lys Phe		
610	615	620
Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys Thr Val Glu Phe Ala Lys		
625	630	635
Gln Leu Pro Gly Phe Thr Thr Leu Thr Ile Ala Asp Gln Ile Thr Leu		
645	650	655
Leu Lys Ala Ala Cys Leu Asp Ile Leu Ile Leu Arg Ile Cys Thr Arg		
660	665	670
Tyr Thr Pro Glu Gln Asp Thr Met Thr Phe Ser Asp Gly Leu Thr Leu		
675	680	685
Asn Arg Thr Gln Met His Met Ala Gly Phe Gly Pro Leu Thr Asp Leu		
690	695	700
Val Phe Ala Phe Ala Asn Gln Leu Leu Pro Leu Glu Met Asp Asp Ala		
705	710	715
		720

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Glu	Thr	Gly	Leu	Leu	Ser	Ala	Ile	Cys	Leu	Ile	Cys	Gly	Asp	Arg	Gln
			725						730					735	
Asp	Leu	Glu		Gln	Pro	Asp	Arg	Val	Asp	Met	Leu	Gln	Glu	Pro	Leu
			740						745					750	
Glu	Ala	Leu	Lys	Val	Tyr	Val	Arg	Lys	Arg	Arg	Pro	Ser	Arg	Pro	His
		755					760					765			
Met	Phe	Pro	Lys	Met	Leu	Met	Lys	Ile	Thr	Asp	Leu	Arg	Ser	Ile	Ser
	770					775					780				
Ala	Lys	Gly	Ala	Glu	Arg	Val	Ile	Thr	Leu	Lys	Met	Glu	Ile	Pro	Gly
	785				790					795					800
Ser	Met	Pro	Pro	Leu	Ile	Gln	Glu	Met	Leu	Glu	Asn	Ser	Glu	Gly	Leu
				805					810					815	
Asp	Thr	Leu	Ser	Gly	Gln	Pro	Gly	Gly	Gly	Arg	Asp		Gly	Gly	Gly
		820					825						830		
Leu	Ala	Pro	Pro	Pro	Gly	Ser	Cys	Ser	Pro	Ser	Leu	Ser	Pro	Ser	Ser
		835					840					845			
Asn	Arg	Ser	Ser	Pro	Ala	Thr	His	Ser	Pro						
	850					855									

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<210> 53
<211> 277
<212> PRT
<213> Homo sapiens
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400> 53
Met Ala Ser Asn Ser Ser Ser Cys Pro Thr Pro Gly Gly Gly His Leu
  1          5          10          15
Asn Gly Tyr Pro Val Pro Pro Tyr Ala Phe Phe Phe Pro Pro Met Leu
  20          25          30
Gly Gly Leu Ser Pro Pro Gly Ala Leu Thr Thr Leu Gln His Gln Leu
  35          40          45
Pro Val Ser Gly Tyr Ser Thr Pro Ser Pro Ala Thr Gly Ala Lys Ala
  50          55          60
Phe Val Cys Asp Gln Cys Gly Ala Gln Phe Ser Lys Glu Asp Ala Leu
  65          70          75          80
Glu Thr His Arg Gln Thr His Thr Gly Thr Asp Met Ala Val Phe Cys
  85          90          95
Leu Leu Cys Gly Lys Arg Phe Gln Ala Gln Ser Ala Leu Gln Gln His
 100          105          110
Met Glu Val His Ala Gly Val Arg Ser Tyr Ile Cys Ser Glu Cys Asn
 115          120          125

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Arg Thr Phe Pro Ser His Thr Ala Leu Lys Arg His Leu Arg Ser His  
130 135 140

Thr Gly Asp His Pro Tyr Glu Cys Glu Phe Cys Gly Ser Cys Phe Arg  
145 150 155 160

Asp Glu Ser Thr Leu Lys Ser His Lys Arg Ile His Thr Gly Glu Lys  
165 170

Pro Tyr Glu Cys Asn Gly Cys Asp Lys Lys Phe Ser Leu Lys His Gln  
180 185 190

Leu Glu Thr His Tyr Arg Val His Thr Gly Glu Lys Pro Phe Glu Cys  
195 200 205

Lys Leu Cys His Gln Arg Ser Arg Asp Tyr Ser Ala Met Ile Lys His  
210 215 220

Leu Arg Thr His Asn Gly Ala Ser Pro Tyr Gln Cys Thr Ile Cys Thr  
225 230 235 240

Glu Tyr Cys Pro Ser Leu Ser Ser Met Gln Lys His Met Lys Gly His  
245 250 255

Lys Pro Glu Glu Ile Pro Pro Asp Trp Arg Ile Glu Lys Thr Tyr Leu  
260 265 270

Tyr Leu Cys Tyr Val  
275

&lt;210&gt; 54

&lt;211&gt; 2311

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 54

Met Ala His Ser Cys Arg Trp Arg Phe Pro Ala Arg Pro Gly Thr Thr  
1 5 10 15

Gly Gly Gly Gly Gly Gly Gly Arg Arg Gly Leu Gly Gly Gly Pro Arg  
20 25 30

Gln Arg Val Pro Ala Leu Leu Leu Pro Pro Gly Pro Pro Val Gly Gly  
35 40 45

Gly Gly Pro Gly Ala Pro Pro Ser Pro Pro Ala Val Ala Ala Ala Ala  
50 55 60

Ala Ala Ala Gly Ser Ser Gly Ala Gly Val Pro Gly Gly Ala Ala Ala  
65 70 75 80

Ala Ser Ala Ala Ser Ser Ser Ser Ala Ser Ser Ser Ser Ser Ser Ser  
85 90 95

Ser Ser Ala Ser Ser Gly Pro Ala Leu Leu Arg Val Gly Pro Gly Phe  
100 105 110

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Asp Ala Ala Leu Gln Val Ser Ala Ala Ile Gly Thr Asn Leu Arg Arg  
 115 120 125  
 Phe Arg Ala Val Phe Gly Glu Ser Gly Gly Gly Gly Ser Gly Glu  
 130 135 140  
 Leu Thr Thr Gln Ile Pro Cys Ser Trp Arg Thr Lys Gly His Ile His  
 145 150 155 160  
 Asp Lys Lys Thr Glu Pro Phe Arg Leu Leu Ala Trp Ser Trp Cys Leu  
 165 170 175  
 Asn Asp Glu Gln Phe Leu Gly Phe Gly Ser Asp Glu Glu Val Arg Val  
 180 185 190  
 Arg Ser Pro Thr Arg Ser Pro Ser Val Lys Thr Ser Pro Arg Lys Pro  
 195 200 205  
 Arg Gly Arg Pro Arg Ser Gly Ser Asp Arg Asn Ser Ala Ile Leu Ser  
 210 215 220  
 Asp Pro Ser Val Phe Ser Pro Leu Asn Lys Ser Glu Thr Lys Ser Gly  
 225 230 235 240  
 Asp Lys Ile Lys Lys Lys Asp Ser Lys Ser Ile Glu Lys Lys Arg Gly  
 245 250 255  
 Arg Pro Pro Thr Phe Pro Gly Val Lys Ile Lys Ile Thr His Gly Lys  
 260 265 270  
 Asp Ile Ser Glu Leu Pro Lys Gly Asn Lys Glu Asp Ser Leu Lys Lys  
 275 280 285  
 Ile Lys Arg Thr Pro Ser Ala Thr Phe Gln Gln Ala Thr Lys Ile Lys  
 290 295 300  
 Lys Leu Arg Ala Gly Lys Leu Ser Pro Leu Lys Ser Lys Phe Lys Thr  
 305 310 315 320  
 Gly Lys Leu Gln Ile Gly Arg Lys Gly Val Gln Ile Val Arg Arg Arg  
 325 330 335  
 Gly Arg Pro Pro Ser Thr Glu Arg Ile Lys Thr Pro Ser Gly Leu Leu  
 340 345 350  
 Ile Asn Ser Glu Leu Glu Lys Pro Gln Lys Val Arg Lys Asp Lys Glu  
 355 360 365  
 Gly Thr Pro Pro Leu Thr Lys Glu Asp Lys Thr Val Val Arg Gln Ser  
 370 375 380  
 Pro Arg Arg Ile Lys Pro Val Arg Ile Ile Pro Ser Ser Lys Arg Thr  
 385 390 395 400  
 Asp Ala Thr Ile Ala Lys Gln Leu Leu Gln Arg Ala Lys Lys Gly Ala  
 405 410 415

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Gln Lys Lys Ile Glu Lys Glu Ala Ala Gln Leu Gln Gly Arg Lys Val  
 420 425 430  
 Lys Thr Gln Val Lys Asn Ile Arg Gln Phe Ile Met Pro Val Val Ser  
 435 440 445  
 Ala Ile Ser Ser Arg Ile Ile Lys Thr Pro Arg Arg Phe Ile Glu Asp  
 450 455 460  
 Glu Asp Tyr Asp Pro Pro Ile Lys Ile Ala Arg Leu Glu Ser Thr Pro  
 465 470 475 480  
 Asn Ser Arg Phe Ser Ala Pro Ser Cys Gly Ser Ser Glu Lys Ser Ser  
 485 490 495  
 Ala Ala Ser Gln His Ser Ser Gln Met Ser Ser Asp Ser Ser Arg Ser  
 500 505 510  
 Ser Ser Pro Ser Val Asp Thr Ser Thr Asp Ser Gln Ala Ser Glu Glu  
 515 520 525  
 Ile Gln Val Leu Pro Glu Glu Arg Ser Asp Thr Pro Glu Val His Pro  
 530 535 540  
 Pro Leu Pro Ile Ser Gln Ser Pro Glu Asn Glu Ser Asn Asp Arg Arg  
 545 550 555 560  
 Ser Arg Arg Tyr Ser Val Ser Glu Arg Ser Phe Gly Ser Arg Thr Thr  
 565 570 575  
 Lys Lys Leu Ser Thr Leu Gln Ser Ala Pro Gln Gln Gln Thr Ser Ser  
 580 585 590  
 Ser Pro Pro Pro Pro Leu Leu Thr Pro Pro Pro Pro Leu Gln Pro Ala  
 595 600 605  
 Ser Ser Ile Ser Asp His Thr Pro Trp Leu Met Pro Pro Thr Ile Pro  
 610 615 620  
 Phe Gly Leu Cys Ser Asn Asn Pro Leu Thr Ser Pro Phe Leu Pro Ala  
 625 630 635 640  
 Ser Thr Ala Pro Met Gln Gly Lys Arg Lys Ser Ile Leu Arg Glu Pro  
 645 650 655  
 Thr Phe Arg Trp Thr Ser Leu Lys His Ser Arg Ser Glu Pro Gln Thr  
 660 665 670  
 Phe Ser Ser Ala Lys Tyr Ala Lys Glu Gly Leu Ile Arg Lys Pro Ile  
 675 680 685  
 Phe Asp Asn Phe Arg Pro Pro Pro Leu Thr Pro Glu Asp Val Gly Phe  
 690 695 700  
 Ala Ser Gly Phe Ser Ala Ser Gly Thr Ala Ala Ser Ala Arg Leu Phe  
 705 710 715 720  
 Ser Pro Leu His Ser Gly Thr Arg Phe Asp Met His Lys Arg Ser Pro

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725	730	735
Leu Leu Arg Ala Pro Arg Phe Thr Pro Ser Glu Ala His Ser Arg Ile 740 745 750		
Phe Glu Ser Val Thr Leu Pro Ser Asn Arg Thr Ser Ala Gly Thr Ser 755 760 765		
Ser Ser Gly Val Ser Asn Arg Lys Arg Lys Arg Lys Val Phe Ser Pro 770 775 780		
Ile Arg Ser Glu Pro Arg Ser Pro Ser His Ser Met Arg Thr Arg Ser 785 790 795 800		
Gly Arg Leu Ser Ser Ser Glu Leu Ser Pro Leu Thr Pro Pro Ser Ser 805 810 815		
Val Ser Ser Ser Leu Ser Ile Ser Val Ser Pro Leu Ala Thr Ser Ala 820 825 830		
Leu Asn Pro Thr Phe Thr Phe Pro Ser His Ser Leu Thr Gln Ser Gly 835 840 845		
Glu Ser Ala Glu Lys Asn Gln Arg Pro Arg Lys Gln Thr Ser Ala Pro 850 855 860		
Ala Glu Pro Phe Ser Ser Ser Ser Pro Thr Pro Leu Phe Pro Trp Phe 865 870 875 880		
Thr Pro Gly Ser Gln Thr Glu Arg Gly Arg Asn Lys Asp Lys Ala Pro 885 890 895		
Glu Glu Leu Ser Lys Asp Arg Asp Ala Asp Lys Ser Val Glu Lys Asp 900 905 910		
Lys Ser Arg Glu Arg Asp Arg Glu Arg Glu Lys Glu Asn Lys Arg Glu 915 920 925		
Ser Arg Lys Glu Lys Arg Lys Lys Gly Ser Glu Ile Gln Ser Ser Ser 930 935 940		
Ala Leu Tyr Pro Val Gly Arg Val Ser Lys Glu Lys Val Val Gly Glu 945 950 955 960		
Asp Val Ala Thr Ser Ser Ser Ala Lys Lys Ala Thr Gly Arg Lys Lys 965 970 975		
Ser Ser Ser His Asp Ser Gly Thr Asp Ile Thr Ser Val Thr Leu Gly 980 985 990		
Asp Thr Thr Ala Val Lys Thr Lys Ile Leu Ile Lys Lys Gly Arg Gly 995 1000 1005		
Asn Leu Glu Lys Thr Asn Leu Asp Leu Gly Pro Thr Ala Pro Ser Leu 1010 1015 1020		
Glu Lys Glu Lys Thr Leu Cys Leu Ser Thr Pro Ser Ser Ser Thr Val 1025 1030 1035 1040		

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Lys His Ser Thr Ser Ser Ile Gly Ser Met Leu Ala Gln Ala Asp Lys  
 1045 1050 1055  
 Leu Pro Met Thr Asp Lys Arg Val Ala Ser Leu Leu Lys Lys Ala Lys  
 1060 1065 1070  
 Ala Gln Leu Cys Lys Ile Glu Lys Ser Lys Ser Leu Lys Gln Thr Asp  
 1075 1080 1085  
 Gln Pro Lys Ala Gln Gly Gln Glu Ser Asp Ser Ser Glu Thr Ser Val  
 1090 1095 1100  
 Arg Gly Pro Arg Ile Lys His Val Cys Arg Arg Ala Ala Val Ala Leu  
 1105 1110 1115 1120  
 Gly Arg Lys Arg Ala Val Phe Pro Asp Asp Met Pro Thr Leu Ser Ala  
 1125 1130 1135  
 Leu Pro Trp Glu Glu Arg Glu Lys Ile Leu Phe Ser Met Gly Asn Asp  
 1140 1145 1150  
 Asp Lys Ser Ser Ile Ala Gly Ser Glu Asp Ala Glu Pro Leu Ala Pro  
 1155 1160 1165  
 Pro Ile Lys Pro Ile Lys Pro Val Thr Arg Asn Lys Ala Pro Gln Glu  
 1170 1175 1180  
 Pro Pro Val Lys Lys Gly Arg Arg Ser Arg Arg Cys Gly Gln Cys Pro  
 1185 1190 1195 1200  
 Gly Cys Gln Val Pro Glu Asp Cys Gly Val Cys Thr Asn Cys Leu Asp  
 1205 1210 1215  
 Lys Pro Lys Phe Gly Gly Arg Asn Ile Lys Lys Gln Cys Cys Lys Met  
 1220 1225 1230  
 Arg Lys Cys Gln Asn Leu Gln Trp Met Pro Ser Lys Ala Tyr Leu Gln  
 1235 1240 1245  
 Lys Gln Ala Lys Ala Val Lys Lys Lys Glu Lys Lys Ser Lys Thr Ser  
 1250 1255 1260  
 Glu Lys Lys Asp Ser Lys Glu Ser Ser Val Val Lys Asn Val Val Asp  
 1265 1270 1275 1280  
 Ser Ser Gln Lys Pro Thr Pro Ser Ala Arg Glu Asp Pro Ala Pro Lys  
 1285 1290 1295  
 Lys Ser Ser Ser Glu Pro Pro Pro Arg Lys Pro Val Glu Glu Lys Ser  
 1300 1305 1310  
 Glu Glu Gly Asn Val Ser Ala Pro Gly Pro Glu Ser Lys Gln Ala Thr  
 1315 1320 1325  
 Thr Pro Ala Ser Arg Lys Ser Ser Lys Gln Val Ser Gln Pro Ala Leu  
 1330 1335 1340

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Val Ile Pro Pro Gln Pro Pro Thr Thr Gly Pro Pro Arg Lys Glu Val  
 1345 1350 1355 1360  
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 Ala Thr Val Pro Arg Val Arg Ser Ile Leu Asn Pro Lys Ile Leu Pro



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 1940                      1945                      1950  
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 1955                      1960                      1965

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Val Pro Ile Thr Pro Arg Val Val Cys Phe Leu Cys Ala Ser Ser Gly

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&lt;210&gt; 69

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 69

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Ile Ser Leu Pro Ser Pro Val Pro Pro Leu Ser Pro Ile His Ser Asn
1 5 10 15

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```

Gln Gln Thr Leu Pro Arg Thr Gln Gly Ser Ser Lys Val His Gly Ser
20 25 30

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```

Ser Asn Asn Ser Lys Gly Tyr Cys Pro Ala Lys Ser Pro Lys Asp Leu
35 40 45

```

```

Ala Val Lys Val His Asp Lys Glu Thr Pro Gln Asp Ser Leu Val Ala
50 55 60

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```

Pro Ala Gln Pro Pro Ser Gln Thr Phe Pro Pro Pro Ser Leu Pro Ser
65 70 75 80

```

```

Lys Ser Val Ala Met Gln Gln Lys Pro Thr Ala Tyr Val Arg Pro Met
85 90 95

```

```

Asp Gly Gln Asp Gln Ala Pro Ser Glu Ser Pro Glu Leu Lys Pro Leu
100 105 110

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```

Pro Glu Asp Tyr Arg Gln Gln Thr Phe Glu Lys Thr Asp Leu Lys Val
115 120 125

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```

Pro Ala Lys Ala Lys Leu Thr Lys Leu Lys Met Pro Ser Gln Ser Val
130 135 140

```

```

Glu Gln Thr Tyr Ser Asn Glu Val His Cys Val Glu Glu Ile Leu Lys
145 150 155 160

```

```

Glu Lys Pro Pro Pro Val Asn Lys Gln Glu Asn Ala Gly Thr Leu Asn
165 170 175

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Ile Leu Ser Thr Leu Ser Asn Gly Asn Ser Ser Lys Gln Lys Ile Pro  
 180 185 190

Ala Asp Gly Val His Arg  
 195

<210> 70  
 <211> 596  
 <212> DNA  
 <213> Homo sapiens

<400> 70  
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 ccagccaaat ctcccaagga cctagcagtg aaagtccatg ataagagac cctccaagac 180  
 agtttgggtg cccctgccca gcgccttct cagacatttc cactccctc cctccctca 240  
 aaaagtgttg caatgcagca gaagcccacg gcttatgttc ggcccatgga tggtaagat 300  
 caggccctca gtgaatcccc tgaactgaaa ccaactgccg aggaactatg acagcagacc 360  
 tttgaaaaaa cagacttgaa agtgccctgc aaagccaagc tcaccaaact gaagatgcct 420  
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 gaaaaaacac ctccggtcaa taagcaggag aatgcaggca ctttgaacat cctcagcact 540  
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<210> 71  
 <211> 198  
 <212> PRT  
 <213> Homo sapiens

<400> 71  
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 Ser Asn Asn Ser Lys Gly Tyr Cys Pro Ala Lys Ser Pro Lys Asp Leu  
 35 40 45  
 Ala Val Lys Val His Asp Lys Glu Thr Pro Gln Asp Ser Leu Val Ala  
 50 55 60  
 Pro Ala Gln Pro Pro Ser Gln Thr Phe Pro Pro Pro Ser Leu Pro Ser  
 65 70 75 80  
 Lys Ser Val Ala Met Gln Gln Lys Pro Thr Ala Tyr Val Arg Pro Met  
 85 90 95  
 Asp Gly Gln Asp Gln Ala Pro Ser Glu Ser Pro Glu Leu Lys Pro Leu  
 100 105 110  
 Pro Glu Asp Tyr Arg Gln Gln Thr Phe Glu Lys Thr Asp Leu Lys Val  
 115 120 125  
 Pro Ala Lys Ala Lys Leu Thr Lys Leu Lys Met Pro Ser Gln Ser Val  
 130 135 140

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Glu Gln Thr Tyr Ser Asn Glu Val His Cys Val Glu Glu Ile Leu Lys  
145 150 155 160

Glu Lys Pro Pro Pro Val Asn Lys Gln Glu Asn Ala Gly Thr Leu Asn  
165 170 175

Ile Leu Ser Thr Leu Ser Asn Gly Asn Ser Ser Lys Gln Lys Ile Pro  
180 185 190

Ala Asp Gly Val His Arg  
195

&lt;210&gt; 72

&lt;211&gt; 596

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 72

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agtttggtag ccctgcccca gcgccttctc cagacatttc cacctccctc cctcccccca 240
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&lt;210&gt; 73

&lt;211&gt; 747

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 73

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agcagagcac tcccaaaccc cttgtaagaa agcatgaaga ataatgcacc tgcacttcag 180
aggccaaatt ttaaacctga aaagatctaa atatagaagt tttaaaatag tgacaggcag 240
gtttttttag gcagaagctg taaaccagca gcctgagggc taggttgggc ctgcagacaa 300
attattttgt ttggcctgta gggcttgttt tctttcttct tccctaccgc cccccacact 360
tttagccagt atttacaac tggagaattt aggaaaaaaa tcattatttg ctgagtagag 420
gcaatttctg gaacctggcc actgtattgc agcctaggca acaagcaag acccagtcct 480
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tttgtctcat attcatcttt tgtctcctta ggaaaaacca cctccggtca atagcagga 660
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aattccagca gatggagtcc acaggat 747
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&lt;210&gt; 74

&lt;211&gt; 2598

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

<400> 74  
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 ggagggcaag aaggaaatgc tgaaccacaa gtactaacaa aaaagcactg atgtctcaaa 180  
 cagcatttga aagcaggaaa tgtatgattt gaagtcttca gttcaagaaa atcagctctc 240  
 tttctaacta taattgtttaa taataaagaa acagaaacaa aaaaaacagt taagtggag 300  
 gtattgtttt aatttccctgt tcgaagccta gagtttaaat agtttttttt ttttttcta 360  
 atggcccttt cttcacagggt cagtcagtc taaagtatgc gttgccagca tctgactgca 420  
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 aagtatccct gtaaaaacaa aaccaaaaga aaaggtgagg agagatttgt ttctctgcc 540  
 tttctcaggg atgtattcta tttttagagg aaaaagccta tcttgaact ctatgtagat 600  
 ggcatggaaa tttcttaaaa ttaagaacct tcaagtttag gcttttagct gggcacggtg 660  
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 aaaaaagaa agaagaagaa gttagccagg catggtggca gttgctgtga gtcccaggta 840  
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 tcaactcttt ccggatcc 2598

&lt;210&gt; 75

&lt;211&gt; 60

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 75

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&lt;210&gt; 76

&lt;211&gt; 74

62/299

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 76

atagctgggc acggtggctc acgcctgtaa tcccagagaga atggtatctt ttactcaagt 60  
 aggtgagttg gtgg 74

&lt;210&gt; 77

&lt;211&gt; 84

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 77

ttccgctccc actagccccc cagatgccac aaaatgttag tgccctatta tcagaggtaa 60  
 ttttaatttct tccattctaa attt 84

&lt;210&gt; 78

&lt;211&gt; 501

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 78

Met	Arg	Ile	Gln	Pro	Gln	Lys	Ala	Ala	Ala	Ile	Ile	Asp	Leu	Asp	Pro
1				5						10				15	
Asp	Phe	Glu	Pro	Gln	Ser	Arg	Pro	Arg	Ser	Cys	Thr	Trp	Pro	Leu	Pro
		20						25					30		
Arg	Pro	Glu	Ile	Ala	Asn	Gln	Pro	Ser	Glu	Pro	Pro	Glu	Val	Glu	Pro
		35					40					45			
Asp	Leu	Gly	Glu	Lys	Val	His	Thr	Glu	Gly	Arg	Ser	Glu	Pro	Ile	Leu
	50					55				60					
Leu	Pro	Ser	Arg	Leu	Ser	Glu	Pro	Ala	Gly	Gly	Pro	Gln	Pro	Gly	Ile
65				70					75					80	
Leu	Gly	Ala	Val	Thr	Gly	Pro	Arg	Lys	Gly	Gly	Ser	Arg	Arg	Asn	Ala
			85					90						95	
Trp	Gly	Asn	Gln	Ser	Tyr	Ala	Glu	Phe	Ile	Ser	Gln	Ala	Ile	Glu	Ser
		100					105						110		
Ala	Pro	Glu	Lys	Arg	Leu	Thr	Leu	Ala	Gln	Ile	Tyr	Glu	Trp	Met	Val
		115					120					125			
Arg	Thr	Val	Pro	Tyr	Phe	Lys	Asp	Lys	Gly	Asp	Ser	Asn	Ser	Ser	Ala
	130					135				140					
Gly	Trp	Lys	Asn	Ser	Ile	Arg	His	Asn	Leu	Ser	Leu	His	Ser	Lys	Phe
145					150					155				160	
Ile	Lys	Val	His	Asn	Glu	Ala	Thr	Gly	Lys	Ser	Ser	Trp	Trp	Met	Leu
		165						170						175	
Asn	Pro	Glu	Gly	Gly	Lys	Ser	Gly	Lys	Ala	Pro	Arg	Arg	Arg	Ala	Ala

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180		185		190
Ser Met Asp Ser Ser Ser Lys Leu Leu Arg Gly Arg Ser Lys Ala Pro				
195		200		205
Lys Lys Lys Pro Ser Val Leu Pro Ala Pro Pro Glu Gly Ala Thr Pro				
210		215		220
Thr Ser Pro Val Gly His Phe Ala Lys Trp Ser Gly Ser Pro Cys Ser				
225		230		240
Arg Asn Arg Glu Glu Ala Asp Met Trp Thr Thr Phe Arg Pro Arg Ser				
	245		250	255
Ser Ser Asn Ala Ser Ser Val Ser Thr Arg Leu Ser Pro Leu Arg Pro				
	260		265	270
Glu Ser Glu Val Leu Ala Glu Glu Ile Pro Ala Ser Val Ser Ser Tyr				
	275		280	285
Ala Gly Gly Val Pro Pro Thr Leu Asn Glu Gly Leu Glu Leu Leu Asp				
	290		295	300
Gly Leu Asn Leu Thr Ser Ser His Ser Leu Ser Arg Ser Gly Leu				
305		310		315
Ser Gly Phe Ser Leu Gln His Pro Gly Val Thr Gly Pro Leu His Thr				
	325		330	335
Tyr Ser Ser Ser Leu Phe Ser Pro Ala Glu Gly Pro Leu Ser Ala Gly				
	340		345	350
Glu Gly Cys Phe Ser Ser Ser Gln Ala Leu Glu Ala Leu Leu Thr Ser				
	355		360	365
Asp Thr Pro Pro Pro Pro Ala Asp Val Leu Met Thr Gln Val Asp Pro				
	370		375	380
Ile Leu Ser Gln Ala Pro Thr Leu Leu Leu Leu Gly Gly Leu Pro Ser				
385		390		395
Ser Ser Lys Leu Ala Thr Gly Val Gly Leu Cys Pro Lys Pro Leu Glu				
	405		410	415
Ala Arg Gly Pro Ser Ser Leu Val Pro Thr Leu Ser Met Ile Ala Pro				
	420		425	430
Pro Pro Val Met Ala Ser Ala Pro Ile Pro Lys Ala Leu Gly Thr Pro				
	435		440	445
Val Leu Thr Pro Pro Thr Glu Ala Ala Ser Gln Asp Arg Met Pro Gln				
	450		455	460
Asp Leu Asp Leu Asp Met Tyr Met Glu Asn Leu Glu Cys Asp Met Asp				
465		470		475
Asn Ile Ile Ser Asp Leu Met Asp Glu Gly Glu Gly Leu Asp Phe Asn				
	485		490	495

Phe Glu Pro Asp Pro  
500

<210> 79  
<211> 3171  
<212> DNA  
<213> Homo sapiens

<400> 79  
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65/299

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taaatgccta taaccagcag aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 3171

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<210> 80  
 <211> 501  
 <212> PRT  
 <213> Homo sapiens

<400> 80  
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 Arg Pro Glu Ile Ala Asn Gln Pro Ser Glu Pro Pro Glu Val Glu Pro  
 35 40 45  
 Asp Leu Gly Glu Lys Val His Thr Glu Gly Arg Ser Glu Pro Ile Leu  
 50 55 60  
 Leu Pro Ser Arg Leu Ser Glu Pro Ala Gly Gly Pro Gln Pro Gly Ile  
 65 70 75 80  
 Leu Gly Ala Val Thr Gly Pro Arg Lys Gly Gly Ser Arg Arg Asn Ala  
 85 90 95  
 Trp Gly Asn Gln Ser Tyr Ala Glu Phe Ile Ser Gln Ala Ile Glu Ser  
 100 105 110  
 Ala Pro Glu Lys Arg Leu Thr Leu Ala Gln Ile Tyr Glu Trp Met Val  
 115 120 125  
 Arg Thr Val Pro Tyr Phe Lys Asp Lys Gly Asp Ser Asn Ser Ser Ala  
 130 135 140  
 Gly Trp Lys Asn Ser Ile Arg His Asn Leu Ser Leu His Ser Lys Phe  
 145 150 155 160  
 Ile Lys Val His Asn Glu Ala Thr Gly Lys Ser Ser Trp Trp Met Leu  
 165 170 175  
 Asn Pro Glu Gly Gly Lys Ser Gly Lys Ala Pro Arg Arg Arg Ala Ala  
 180 185 190  
 Ser Met Asp Ser Ser Ser Lys Leu Leu Arg Gly Arg Ser Lys Ala Pro  
 195 200 205  
 Lys Lys Lys Pro Ser Val Leu Pro Ala Pro Pro Glu Gly Ala Thr Pro  
 210 215 220  
 Thr Ser Pro Val Gly His Phe Ala Lys Trp Ser Gly Ser Pro Cys Ser  
 225 230 235 240



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Arg Asn Arg Glu Glu Ala Asp Met Trp Thr Thr Phe Arg Pro Arg Ser  
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 Ser Ser Asn Ala Ser Ser Val Ser Thr Arg Leu Ser Pro Leu Arg Pro  
 260 265 270  
 Glu Ser Glu Val Leu Ala Glu Glu Ile Pro Ala Ser Val Ser Ser Tyr  
 275 280 285  
 Ala Gly Gly Val Pro Pro Thr Leu Asn Glu Gly Leu Glu Leu Asp  
 290 295 300  
 Gly Leu Asn Leu Thr Ser Ser His Ser Leu Leu Ser Arg Ser Gly Leu  
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 Ser Gly Phe Ser Ser Leu Gln His Pro Gly Val Thr Gly Pro Leu His Thr  
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 Tyr Ser Ser Ser Leu Phe Ser Pro Ala Glu Gly Pro Leu Ser Ala Gly  
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 Glu Gly Cys Phe Ser Ser Ser Gln Ala Leu Glu Ala Leu Leu Thr Ser  
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 Asp Thr Pro Pro Pro Pro Ala Asp Val Leu Met Thr Gln Val Asp Pro  
 370 375 380  
 Ile Leu Ser Gln Ala Pro Thr Leu Leu Leu Leu Gly Gly Leu Pro Ser  
 385 390 395 400  
 Ser Ser Lys Leu Ala Thr Gly Val Gly Leu Cys Pro Lys Pro Leu Glu  
 405 410 415  
 Ala Arg Gly Pro Ser Ser Leu Val Pro Thr Leu Ser Met Ile Ala Pro  
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 435 440 445  
 Val Leu Thr Pro Pro Thr Glu Ala Ala Ser Gln Asp Arg Met Pro Gln  
 450 455 460  
 Asp Leu Asp Leu Asp Met Tyr Met Glu Asn Leu Glu Cys Asp Met Asp  
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<210> 81  
 <211> 3171  
 <212> DNA  
 <213> Homo sapiens

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tcccocaaac ctgctgtggg tcccactcat ttccgtgtgc aggcctcggc ctaccagagt 3060
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3171

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&lt;210&gt; 82

&lt;211&gt; 74

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<212> DNA  
<213> Homo sapiens

<400> 82  
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ggaacctctg caga 74

<210> 83  
<211> 22  
<212> PRT  
<213> Homo sapiens

<400> 83  
Lys Gln Pro Pro Pro Glu Ser Gly Phe Gly Val Pro Trp Ser Asp  
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Glu Ile Leu Phe Ser Arg  
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<210> 84  
<211> 69  
<212> DNA  
<213> Homo sapiens

<400> 84  
aagcagcctc caccaccaga atcaggattt ggagttccat ggagtgatga gattttattt 60  
tcaagataa 69

<210> 85  
<211> 23  
<212> PRT  
<213> Homo sapiens

<400> 85  
Val Lys Gln Lys Pro Lys Glu Lys Asp Leu Glu Phe His Gly Val Met  
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Arg Phe Tyr Phe Gln Asp Lys  
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<210> 86  
<211> 69  
<212> DNA  
<213> Homo sapiens

<400> 86  
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caagataaa 69

<210> 87  
<211> 23  
<212> PRT  
<213> Homo sapiens

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<400> 87  
His Arg Ile Arg Val Asp Phe Lys Asp Leu Glu Phe His Gly Val Met  
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Arg Phe Tyr Phe Gln Asp Lys  
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<210> 88  
<211> 69  
<212> DNA  
<213> Homo sapiens

<400> 88  
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caagataaaa 69

<210> 89  
<211> 76  
<212> PRT  
<213> Homo sapiens

<400> 89  
Pro Pro Thr Thr Gly Pro Pro Arg Lys Glu Val Pro Lys Thr Thr Pro  
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Ser Glu Pro Lys Lys Lys Gln Pro Pro Pro Glu Ser Gly Ile Tyr  
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Thr Ser Asn Lys Asp Pro Ile Ser His Ser Gly Gly Met Leu Arg Ala  
35 40 45

Val Cys Ser Thr Pro Leu Ser Ser Ser Leu Leu Gly Pro Pro Gly Thr  
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Ser Ala Leu Pro Arg Leu Ser Arg Ser Pro Phe Thr  
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<210> 90  
<211> 228  
<212> DNA  
<213> Homo sapiens

<400> 90  
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cacagtggcg ggaatgctgc ggctgtctgc agcacccttc tctctccag cctcctgggg 180  
ccccaggga cctcggccct gccccgcctc agcgcctccc cgttcacc 228

<210> 91  
<211> 1093  
<212> PRT  
<213> Homo sapiens

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&lt;400&gt; 91

Met Lys Glu Met Val Gly Gly Cys Cys Val Cys Ser Asp Glu Arg Gly  
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Trp Ala Glu Asn Pro Leu Val Tyr Cys Asp Gly His Ala Cys Ser Val  
 20 25 30

Ala Val His Gln Ala Cys Tyr Gly Ile Val Gln Val Pro Thr Gly Pro  
 35 40 45

Trp Phe Cys Arg Lys Cys Glu Ser Gln Glu Arg Ala Ala Arg Val Arg  
 50 55 60

Cys Glu Leu Cys Pro His Lys Asp Gly Ala Leu Lys Arg Thr Asp Asn  
 65 70 75 80

Gly Gly Trp Ala His Val Val Cys Ala Leu Tyr Ile Pro Glu Val Gln  
 85 90 95

Phe Ala Asn Val Leu Thr Met Glu Pro Ile Val Leu Gln Tyr Val Pro  
 100 105 110

His Asp Arg Phe Asn Lys Thr Cys Tyr Ile Cys Glu Glu Thr Gly Arg  
 115 120 125

Glu Ser Lys Ala Ala Ser Gly Ala Cys Met Thr Cys Asn Arg His Gly  
 130 135 140

Cys Arg Gln Ala Phe His Val Thr Cys Ala Gln Met Ala Gly Leu Leu  
 145 150 155 160

Cys Glu Glu Glu Val Leu Glu Val Asp Asn Val Lys Tyr Cys Gly Tyr  
 165 170 175

Cys Lys Tyr His Phe Ser Lys Met Lys Thr Ser Arg His Ser Ser Gly  
 180 185 190

Gly Gly Gly Gly Gly Ala Gly Gly Gly Gly Ser Met Gly Gly Gly  
 195 200 205

Gly Ser Gly Phe Ile Ser Gly Arg Arg Ser Arg Ser Ala Ser Pro Ser  
 210 215 220

Thr Gln Gln Glu Lys His Pro Thr His His Glu Arg Gly Gln Lys Lys  
 225 230 235 240

Ser Arg Lys Asp Lys Glu Arg Leu Lys Gln Lys His Lys Lys Arg Pro  
 245 250 255

Glu Ser Pro Pro Ser Ile Leu Thr Pro Pro Val Val Pro Thr Ala Asp  
 260 265 270

Lys Val Ser Ser Ser Ala Ser Ser Ser Ser His His Glu Ala Ser Thr  
 275 280 285

Gln Glu Thr Ser Glu Ser Ser Arg Glu Ser Lys Gly Lys Lys Ser Ser  
 290 295 300

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Ser His Ser Leu Ser His Lys Gly Lys Lys Leu Ser Ser Gly Lys Gly  
 305 310 315 320  
 Val Ser Ser Phe Thr Ser Ala Ser Ser Ser Ser Ser Ser Ser Ser  
 325 330 335  
 Ser Ser Gly Gly Pro Phe Gln Pro Ala Val Ser Ser Leu Gln Ser Ser  
 340 345 350  
 Pro Asp Phe Ser Ala Phe Pro Lys Leu Glu Gln Pro Glu Glu Asp Lys  
 355 360 365  
 Tyr Ser Lys Pro Thr Ala Pro Ala Pro Ser Ala Pro Pro Ser Pro Ser  
 370 375 380  
 Ala Pro Glu Pro Pro Lys Ala Asp Leu Phe Glu Gln Lys Val Val Phe  
 385 390 395 400  
 Ser Gly Phe Gly Pro Ile Met Arg Phe Ser Thr Thr Thr Ser Ser Ser  
 405 410 415  
 Gly Arg Ala Arg Ala Pro Ser Pro Gly Asp Tyr Lys Ser Pro His Val  
 420 425 430  
 Thr Gly Ser Gly Ala Ser Ala Gly Thr His Lys Arg Met Pro Ala Leu  
 435 440 445  
 Ser Ala Thr Pro Val Pro Ala Asp Glu Thr Pro Glu Thr Gly Leu Lys  
 450 455 460  
 Glu Lys Lys His Lys Ala Ser Lys Arg Ser Arg His Gly Pro Gly Arg  
 465 470 475 480  
 Pro Lys Gly Ser Arg Asn Lys Glu Gly Thr Gly Gly Pro Ala Ala Pro  
 485 490 495  
 Ser Leu Pro Ser Ala Gln Leu Ala Gly Phe Thr Ala Thr Ala Ala Ser  
 500 505 510  
 Pro Phe Ser Gly Gly Ser Leu Val Ser Ser Gly Leu Gly Gly Leu Ser  
 515 520 525  
 Ser Arg Thr Phe Gly Pro Ser Gly Ser Leu Pro Ser Leu Ser Leu Glu  
 530 535 540  
 Ser Pro Leu Leu Gly Ala Gly Ile Tyr Thr Ser Asn Lys Asp Pro Ile  
 545 550 555 560  
 Ser His Ser Gly Gly Met Leu Arg Ala Val Cys Ser Thr Pro Leu Ser  
 565 570 575  
 Ser Ser Leu Leu Gly Pro Pro Gly Thr Ser Ala Leu Pro Arg Leu Ser  
 580 585 590  
 Arg Ser Pro Phe Thr Ser Thr Leu Pro Ser Ser Ser Ala Ser Ile Ser  
 595 600 605  
 Thr Thr Gln Val Phe Ser Leu Ala Gly Ser Thr Phe Ser Leu Pro Ser

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610	615	620
Thr His Ile Phe Gly Thr Pro Met Gly Ala Val Asn Pro Leu Leu Ser		
625	630	635 640
Gln Ala Glu Ser Ser His Thr Glu Pro Asp Leu Glu Asp Cys Ser Phe		
	645	650 655
Arg Cys Arg Gly Thr Ser Pro Gln Glu Ser Leu Ser Ser Met Ser Pro		
	660	665 670
Ile Ser Ser Leu Pro Ala Leu Phe Asp Gln Thr Ala Ser Ala Pro Cys		
	675	680 685
Gly Gly Gly Gln Leu Asp Pro Glu Ala Ala Pro Gly Thr Thr Asn Met Glu		
	690	695 700
Gln Leu Leu Glu Lys Gln Gly Asp Gly Glu Ala Gly Val Asn Ile Val		
705	710	715 720
Glu Met Leu Lys Ala Leu His Ala Leu Gln Lys Glu Asn Gln Arg Leu		
	725	730 735
Gln Glu Gln Ile Leu Ser Leu Thr Ala Lys Lys Glu Arg Leu Gln Ile		
	740	745 750
Leu Asn Val Gln Leu Ser Val Pro Phe Pro Ala Leu Pro Ala Ala Leu		
	755	760 765
Pro Ala Ala Asn Gly Pro Val Pro Gly Pro Tyr Gly Leu Pro Pro Gln		
	770	775 780
Ala Gly Ser Ser Asp Ser Leu Ser Thr Ser Lys Ser Pro Pro Gly Lys		
785	790	795 800
Ser Ser Leu Gly Leu Asp Asn Ser Leu Ser Thr Ser Ser Glu Asp Pro		
	805	810 815
His Ser Gly Cys Pro Ser Arg Ser Ser Ser Ser Leu Ser Phe His Ser		
	820	825 830
Thr Pro Pro Pro Leu Pro Leu Gln Gln Ser Pro Ala Thr Leu Pro		
	835	840 845
Leu Ala Leu Pro Gly Ala Pro Ala Pro Leu Pro Pro Gln Pro Gln Asn		
	850	855 860
Gly Leu Gly Arg Ala Pro Gly Ala Ala Gly Leu Gly Ala Met Pro Met		
865	870	875 880
Ala Glu Gly Leu Leu Gly Gly Leu Ala Gly Ser Gly Gly Leu Pro Leu		
	885	890 895
Asn Gly Leu Leu Gly Gly Leu Asn Gly Ala Ala Ala Pro Asn Pro Ala		
	900	905 910
Ser Leu Ser Gln Ala Gly Gly Ala Pro Thr Leu Gln Leu Pro Gly Cys		
	915	920 925

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Leu Asn Ser Leu Thr Glu Gln Gln Arg His Leu Leu Gln Gln Gln Glu  
930 935 940

Gln Gln Leu Gln Gln Leu Gln Gln Leu Leu Ala Ser Pro Gln Leu Thr  
945 950 955 960

Pro Glu His Gln Thr Val Val Tyr Gln Met Ile Gln Gln Ile Gln Gln  
965 970 975

Lys Arg Glu Leu Gln Arg Leu Gln Met Ala Gly Gly Ser Gln Leu Pro  
980 985 990

Met Ala Ser Leu Leu Ala Gly Ser Ser Thr Pro Leu Leu Ser Ala Gly  
995 1000 1005

Thr Pro Gly Leu Leu Pro Thr Ala Ser Ala Pro Pro Leu Leu Pro Ala  
1010 1015 1020

Gly Ala Leu Val Ala Pro Ser Leu Gly Asn Asn Thr Ser Leu Met Ala  
1025 1030 1035 1040

Ala Ala Ala Ala Ala Ala Ala Val Ala Ala Ala Gly Gly Pro Pro Val  
1045 1050 1055

Leu Thr Ala Gln Thr Asn Pro Phe Leu Ser Leu Ser Gly Ala Glu Gly  
1060 1065 1070

Ser Gly Gly Gly Pro Lys Gly Gly Thr Ala Asp Lys Gly Ala Ser Ala  
1075 1080 1085

Asn Gln Glu Lys Gly  
1090

<210> 92  
<211> 3282  
<212> DNA  
<213> Homo sapiens

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&lt;210&gt; 93

&lt;211&gt; 752

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 93

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Met Arg Ile Pro Val Asp Ala Ser Thr Ser Arg Arg Phe Thr Pro Pro
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Ser Thr Ala Leu Ser Pro Gly Lys Met Ser Glu Ala Leu Pro Leu Gly
      20             25             30

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Ala Pro Asp Ala Gly Ala Ala Leu Ala Gly Lys Leu Arg Ser Gly Asp
      35             40             45

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Arg Ser Met Val Glu Val Leu Ala Asp His Pro Gly Glu Leu Val Arg
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Thr Asp Ser Pro Asn Phe Leu Cys Ser Val Leu Pro Thr His Trp Arg  
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 Val Pro Asp Gly Thr Leu Val Thr Val Met Ala Gly Asn Asp Glu Asn  
 100 105 110  
 Tyr Ser Ala Glu Leu Arg Asn Ala Thr Ala Ala Met Lys Asn Gln Val  
 115 120 125  
 Ala Arg Phe Asn Asp Leu Arg Phe Val Gly Arg Ser Gly Arg Gly Lys  
 130 135 140  
 Ser Phe Thr Leu Thr Ile Thr Val Phe Thr Asn Pro Pro Gln Val Ala  
 145 150 155 160  
 Thr Tyr His Arg Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro  
 165 170 175  
 Arg Asn Arg Thr Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp  
 180 185 190  
 Val Lys Thr Gln Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro  
 195 200 205  
 Thr Thr Gln Gly Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu  
 210 215 220  
 Thr Asn Gly Thr Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser  
 225 230 235 240  
 Pro Pro Asn Gly Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser  
 245 250 255  
 Leu Ala Asn Gln Gln Leu Pro Pro Ala Cys Gly Ala Arg Gln Leu Ser  
 260 265 270  
 Lys Leu Lys Arg Phe Leu Thr Thr Leu Gln Gln Phe Gly Asn Asp Ile  
 275 280 285  
 Ser Pro Glu Ile Gly Glu Arg Val Arg Thr Leu Val Leu Gly Leu Val  
 290 295 300  
 Asn Ser Thr Leu Thr Ile Glu Glu Phe His Ser Lys Leu Gln Glu Ala  
 305 310 315 320  
 Thr Asn Phe Pro Leu Arg Pro Phe Val Ile Pro Phe Leu Lys Ala Asn  
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 340 345 350  
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 355 360 365  
 Ala Ser Thr Thr Ser Pro Val Asp Ser Ser Glu Leu Leu Asp Val

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370	375	380
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385	390	400
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	405	415
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	420	430
Gln Pro Asn Gly Leu Pro His Pro Thr Pro Pro Pro Pro Gln His Tyr		
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Arg Leu Asp Asp Met Ala Ile Ala His His Tyr Arg Asp Ser Tyr Arg		
	450	460
His Pro Ser His Arg Asp Leu Arg Asp Arg Asn Arg Pro Met Gly Leu		
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His Gly Thr Arg Gln Glu Glu Met Ile Asp His Arg Leu Thr Asp Arg		
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Cys Gln Glu Ala Asp Arg Glu Glu Leu Asn Tyr Trp Ile Arg Arg Tyr		
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Ser Asp Ala Glu Asp Leu Lys Lys Gly Gly Ser Ser Ser Ser His		
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Asp Met Ile Thr Thr Glu Arg Ala Lys Met Glu Arg Thr Val Ala Glu		
	625	635
Ala Lys Arg Gln Ala Ala Glu Asp Ala Leu Ala Val Ile Asn Gln Gln		
	645	655
Glu Asp Ser Ser Glu Ser Cys Trp Asn Cys Gly Arg Lys Ala Ser Glu		
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Thr Cys Ser Gly Cys Asn Thr Ala Arg Tyr Cys Gly Ser Phe Cys Gln		
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		680

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His Lys Asp Trp Glu Lys His His His Ile Cys Gly Gln Thr Leu Gln  
690 695 700

Ala Gln Gln Gln Gly Asp Thr Pro Ala Val Ser Ser Ser Val Thr Pro  
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<210> 94

<211> 4272

<212> DNA

<213> Homo sapiens

<400> 94

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&lt;210&gt; 95

&lt;211&gt; 588

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 95

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Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp Val Lys Thr Gln  
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Ser Arg Leu Thr Pro Thr Met Pro Pro Pro Thr Thr Gln Gly  
35 40 45

Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu Thr Asn Gly Thr  
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Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser Pro Pro Asn Gly  
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Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Leu Ala Asn Gln

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85	90	95
Gln Leu Pro	Pro Ala Cys Gly Ala Arg Gln Leu Ser Lys Leu Lys Arg	
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Gly Glu Arg Val	Arg Thr Leu Val Leu Gly Leu Val Asn Ser Thr Leu	
130	135	140
Thr Ile Glu Glu	Phe His Ser Lys Leu Gln Glu Ala Thr Asn Phe Pro	
145	150	155
Leu Arg Pro Phe	Val Ile Pro Phe Leu Lys Ala Asn Leu Pro Leu Leu	
165	170	175
Gln Arg Glu Leu	Leu His Cys Ala Arg Leu Ala Lys Gln Asn Pro Ala	
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Gln Tyr Leu Ala	Gln His Glu Gln Leu Leu Leu Asp Ala Ser Thr Thr	
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Ser Pro Val Asp	Ser Ser Glu Leu Leu Leu Asp Val Asn Glu Asn Gly	
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Lys Arg Arg Thr	Pro Asp Arg Thr Lys Glu Asn Gly Phe Asp Arg Glu	
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Pro Leu His Ser	Glu His Pro Ser Lys Arg Pro Cys Thr Ile Ser Pro	
245	250	255
Gly Gln Arg Tyr	Ser Pro Asn Asn Gly Leu Ser Tyr Gln Pro Asn Gly	
260	265	270
Leu Pro His Pro	Thr Pro Pro Pro Gln His Tyr Arg Leu Asp Asp	
275	280	285
Met Ala Ile Ala	His His Tyr Arg Asp Ser Tyr Arg His Pro Ser His	
290	295	300
Arg Asp Leu Arg	Asp Arg Asn Arg Pro Met Gly Leu His Gly Thr Arg	
305	310	315
Gln Glu Glu Met	Ile Asp His Arg Leu Thr Asp Arg Glu Trp Ala Glu	
325	330	335
Glu Trp Lys His	Leu Asp His Leu Leu Asn Cys Ile Met Asp Met Val	
340	345	350
Glu Lys Thr Arg	Arg Ser Leu Thr Val Leu Arg Arg Cys Gln Glu Ala	
355	360	365
Asp Arg Glu Glu	Leu Asn Tyr Trp Ile Arg Arg Tyr Ser Asp Ala Glu	
370	375	380
Asp Leu Lys Lys	Gly Gly Gly Ser Ser Ser Ser His Ser Arg Gln Gln	
385	390	395
		400

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Ser Pro Val Asn Pro Asp Pro Val Ala Leu Asp Ala His Arg Glu Phe  
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Leu His Arg Pro Ala Ser Gly Tyr Val Pro Glu Glu Ile Trp Lys Lys  
420 425 430

Ala Glu Glu Ala Val Asn Glu Val Lys Arg Gln Ala Met Thr Glu Leu  
435 440 445

Gln Lys Ala Val Ser Glu Ala Glu Arg Lys Ala His Asp Met Ile Thr  
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Thr Glu Arg Ala Lys Met Glu Arg Thr Val Ala Glu Ala Lys Arg Gln  
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Ala Ala Glu Asp Ala Leu Ala Val Ile Asn Gln Gln Glu Asp Ser Ser  
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Glu Ser Cys Trp Asn Cys Gly Arg Lys Ala Ser Glu Thr Cys Ser Gly  
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Cys Asn Thr Ala Arg Tyr Cys Gly Ser Phe Cys Gln His Lys Asp Trp  
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Glu Lys His His His Ile Cys Gly Gln Thr Leu Gln Ala Gln Gln Gln  
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Gly Asp Thr Pro Ala Val Ser Ser Ser Val Thr Pro Asn Ser Gly Ala  
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<211> 2217  
<212> DNA  
<213> Homo sapiens

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&lt;210&gt; 97

&lt;211&gt; 231

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 97

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Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp Val Lys Thr Gln  
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Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Thr Thr Gln Gly  
 35 40 45

Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu Thr Asn Gly Thr  
 50 55 60

Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser Pro Pro Asn Gly  
 65 70 75 80

Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Arg Leu Ala Asn Gln  
 85 90 95

Gln Leu Pro Pro Ala Cys Gly Ala Arg Gln Leu Ser Lys Leu Lys Arg  
 100 105 110

Phe Leu Thr Thr Leu Gln Gln Phe Gly Asn Asp Ile Ser Pro Gln Ile  
 115 120 125

Gly Glu Arg Val Arg Thr Leu Val Leu Gly Leu Val Asn Ser Thr Leu  
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Thr Ile Glu Glu Phe His Ser Lys Leu Gln Glu Ala Thr Asn Phe Pro  
 145 150 155 160

Leu Arg Pro Phe Val Ile Pro Phe Leu Lys Ala Asn Leu Pro Leu Leu  
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Gln Arg Glu Leu Leu His Cys Ala Arg Leu Ala Lys Gln Asn Pro Ala  
 180 185 190

Gln Tyr Leu Ala Gln His Glu Gln Leu Leu Leu Asp Ala Ser Thr Thr  
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Ser Pro Val Asp Ser Ser Glu Leu Leu Leu Asp Val Asn Glu Asn Gly  
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Lys Arg Arg Thr Pro Asp Arg  
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<210> 98  
 <211> 1412  
 <212> DNA  
 <213> Homo sapiens

<400> 98  
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 <211> 198  
 <212> PRT  
 <213> Homo sapiens

<400> 99  
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Arg Asn Arg Thr Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp	35	40	45
Val Lys Thr Gln Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro	50	55	60
Thr Thr Gln Gly Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu	65	70	75
Thr Asn Gly Thr Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser	85	90	95
Pro Pro Asn Gly Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser	100	105	110
Leu Ala Asn Gln Gln Leu Pro Pro Ala Cys Gly Ala Arg Gln Leu Ser	115	120	125
Lys Leu Lys Arg Phe Leu Thr Thr Leu Gln Gln Phe Gly Asn Asp Ile	130	135	140
Ser Pro Glu Ile Gly Glu Arg Val Arg Thr Leu Val Leu Gly Leu Val	145	150	155
Asn Ser Thr Leu Thr Ile Glu Glu Phe His Ser Lys Leu Gln Glu Ala	165	170	175
Thr Asn Phe Pro Leu Arg Pro Phe Val Ile Pro Phe Leu Lys Val Leu	180	185	190
His Ser Ser Leu Val Val	195		

&lt;210&gt; 100

&lt;211&gt; 799

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 100

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gaagaagagt ttagaagtc

799

&lt;210&gt; 101

&lt;211&gt; 237

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 101

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 agctccaaga accagttcat ttacaccgac aacgttaact aatggcacga gccattctcc 180  
 tacagccttg aatggcgccc cctcaccacc caatggcttc agcaatgggc ctctctc 237

&lt;210&gt; 102

&lt;211&gt; 276

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 102

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 aaccccactt gaaaaactga ggtgcttaag gactaaaata atatgttcct ggtggcatcc 180  
 tccagatcgt actgagaagc actccacaat gccagactca cctgtgggatg tgaagacgca 240  
 attcaggctg actcctccaa caatgccacc tcccc 276

&lt;210&gt; 103

&lt;211&gt; 251

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 103

Ser Phe Thr Leu Thr Ile Thr Val Phe Thr Asn Pro Pro Gln Val Ala  
 1 5 10 15

Thr Tyr His Arg Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro  
 20 25 30

Arg Asn Arg Thr Glu Lys His Ser Thr Met Pro Asp Ser Pro Val Asp  
 35 40 45

Val Lys Thr Gln Ser Arg Leu Thr Pro Pro Thr Met Pro Pro Pro Pro  
 50 55 60

Thr Thr Gln Gly Ala Pro Arg Thr Ser Ser Phe Thr Pro Thr Thr Leu  
 65 70 75 80

Thr Asn Gly Thr Ser His Ser Pro Thr Ala Leu Asn Gly Ala Pro Ser  
 85 90 95

Pro Pro Asn Gly Phe Ser Asn Gly Pro Ser Ser Ser Ser Ser Ser Ser  
 100 105 110

Leu Ala Asn Gln Gln Leu Pro Pro Ala Cys Gly Ala Arg Gln Leu Ser  
 115 120 125

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Lys Leu Lys Arg Phe Leu Thr Thr Leu Gln Gln Phe Gly Asn Asp Ile  
130 135 140

Ser Pro Glu Ile Gly Glu Arg Val Arg Thr Leu Val Leu Gly Leu Val  
145 150 155 160

Asn Ser Thr Leu Thr Ile Glu Glu Phe His Ser Lys Leu Gln Glu Ala  
165 170 175

Thr Asn Phe Pro Leu Arg Pro Phe Val Ile Pro Phe Leu Lys Ala Asn  
180 185 190

Leu Pro Leu Leu Gln Arg Glu Leu Leu His Cys Ala Arg Leu Ala Lys  
195 200 205

Gln Asn Pro Ala Gln Tyr Leu Ala Gln His Glu Gln Leu Leu Leu Asp  
210 215 220

Ala Ser Thr Thr Ser Pro Val Asp Ser Ser Glu Leu Leu Leu Asp Val  
225 230 235 240

Asn Glu Asn Gly Lys Arg Arg Thr Pro Asp Arg  
245 250

&lt;210&gt; 104

&lt;211&gt; 1446

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 104

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1446

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&lt;210&gt; 105

&lt;211&gt; 1395

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 105

Met Arg Ile Pro Val Asp Ala Ser Thr Ser Arg Arg Phe Thr Pro Pro  
 1 5 10 15

Ser Thr Ala Leu Ser Pro Gly Lys Met Ser Glu Ala Leu Pro Leu Gly  
 20 25 30

Ala Pro Asp Ala Gly Ala Ala Leu Ala Gly Lys Leu Arg Ser Gly Asp  
 35 40 45

Arg Ser Met Val Glu Val Leu Ala Asp His Pro Gly Glu Leu Val Arg  
 50 55 60

Thr Asp Ser Pro Asn Phe Leu Cys Ser Val Leu Pro Thr His Trp Arg  
 65 70 75 80

Cys Asn Lys Thr Leu Pro Ile Ala Phe Lys Val Val Ala Leu Gly Asp  
 85 90 95

Val Pro Asp Gly Thr Leu Val Thr Val Met Ala Gly Asn Asp Glu Asn  
 100 105 110

Tyr Ser Ala Glu Leu Arg Asn Ala Thr Ala Ala Met Lys Asn Gln Val  
 115 120 125

Ala Arg Phe Asn Asp Leu Arg Phe Val Gly Arg Ser Gly Arg Gly Lys  
 130 135 140

Ser Phe Thr Leu Thr Ile Thr Val Phe Thr Asn Pro Pro Gln Val Ala  
 145 150 155 160

Thr Tyr His Arg Ala Ile Lys Ile Thr Val Asp Gly Pro Arg Glu Pro  
 165 170 175

Arg Asn Asn Glu Cys Val Tyr Gly Asn Tyr Pro Glu Ile Pro Leu Glu  
 180 185 190

Glu Met Pro Asp Ala Asp Gly Val Ala Ser Thr Pro Ser Leu Asn Ile  
 195 200 205

Gln Glu Pro Cys Ser Pro Ala Thr Ser Ser Glu Ala Phe Thr Pro Lys  
 210 215 220

Glu Gly Ser Pro Tyr Lys Ala Pro Ile Tyr Ile Pro Asp Asp Ile Pro  
 225 230 235 240

Ile Pro Ala Glu Phe Glu Leu Arg Glu Ser Asn Met Pro Gly Ala Gly  
 245 250 255

Leu Gly Ile Trp Thr Lys Arg Lys Ile Glu Val Gly Glu Lys Phe Gly  
 260 265 270

Pro Tyr Val Gly Glu Gln Arg Ser Asn Leu Lys Asp Pro Ser Tyr Gly

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275	280	285
Trp Glu Ile Leu Asp Glu Phe Tyr Asn Val Lys Phe Cys Ile Asp Ala		
290	295	300
Ser Gln Pro Asp Val Gly Ser Trp Leu Lys Tyr Ile Arg Phe Ala Gly		
305	310	315
Cys Tyr Asp Gln His Asn Leu Val Ala Cys Gln Ile Asn Asp Gln Ile		
	325	330
		335
Phe Tyr Arg Val Val Ala Asp Ile Ala Pro Gly Glu Glu Leu Leu Leu		
	340	345
		350
Phe Met Lys Ser Glu Asp Tyr Pro His Glu Thr Met Ala Pro Asp Ile		
	355	360
		365
His Glu Glu Arg Gln Tyr Arg Cys Glu Asp Cys Asp Gln Leu Phe Glu		
	370	375
		380
Ser Lys Ala Glu Leu Ala Asp His Gln Lys Phe Pro Cys Ser Thr Pro		
385	390	395
		400
His Ser Ala Phe Ser Met Val Glu Glu Asp Phe Gln Gln Lys Leu Glu		
	405	410
		415
Ser Glu Asn Asp Leu Gln Glu Ile His Thr Ile Gln Glu Cys Lys Glu		
	420	425
		430
Cys Asp Gln Val Phe Pro Asp Leu Gln Ser Leu Glu Lys His Met Leu		
	435	440
		445
Ser His Thr Glu Glu Arg Glu Tyr Lys Cys Asp Gln Cys Pro Lys Ala		
	450	455
		460
Phe Asn Trp Lys Ser Asn Leu Ile Arg His Gln Met Ser His Asp Ser		
465	470	475
		480
Gly Lys His Tyr Glu Cys Glu Asn Cys Ala Lys Val Phe Thr Asp Pro		
	485	490
		495
Ser Asn Leu Gln Arg His Ile Arg Ser Gln His Val Gly Ala Arg Ala		
	500	505
		510
His Ala Cys Pro Glu Cys Gly Lys Thr Phe Ala Thr Ser Ser Gly Leu		
	515	520
		525
Lys Gln His Lys His Ile His Ser Ser Val Lys Pro Phe Ile Cys Glu		
	530	535
		540
Val Cys His Lys Ser Tyr Thr Gln Phe Ser Asn Leu Cys Arg His Lys		
545	550	555
		560
Arg Met His Ala Asp Cys Arg Thr Gln Ile Lys Cys Lys Asp Cys Gly		
	565	570
		575
Gln Met Phe Ser Thr Thr Ser Ser Leu Asn Lys His Arg Arg Phe Cys		
	580	585
		590

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Glu Gly Lys Asn His Phe Ala Ala Gly Gly Phe Phe Gly Gln Gly Ile  
 595 600 605  
 Ser Leu Pro Gly Thr Pro Ala Met Asp Lys Thr Ser Met Val Asn Met  
 610 615 620  
 Ser His Ala Asn Pro Gly Leu Ala Asp Tyr Phe Gly Ala Asn Arg His  
 625 630 635 640  
 Pro Ala Gly Leu Thr Phe Pro Thr Ala Pro Gly Phe Ser Phe Ser Phe  
 645 650 655  
 Pro Gly Leu Phe Pro Ser Gly Leu Tyr His Arg Pro Pro Leu Ile Pro  
 660 665 670  
 Ala Ser Ser Pro Val Lys Gly Leu Ser Ser Thr Glu Gln Thr Asn Lys  
 675 680 685  
 Ser Gln Ser Pro Leu Met Thr His Pro Gln Ile Leu Pro Ala Thr Gln  
 690 695 700  
 Asp Ile Leu Lys Ala Leu Ser Lys His Pro Ser Val Gly Asp Asn Lys  
 705 710 715 720  
 Pro Val Glu Leu Gln Pro Glu Arg Ser Ser Glu Glu Arg Pro Phe Glu  
 725 730 735  
 Lys Ile Ser Asp Gln Ser Glu Ser Ser Asp Leu Asp Asp Val Ser Thr  
 740 745 750  
 Pro Ser Gly Ser Asp Leu Glu Thr Thr Ser Gly Ser Asp Leu Glu Ser  
 755 760 765  
 Asp Ile Glu Ser Asp Lys Glu Lys Phe Lys Glu Asn Gly Lys Met Phe  
 770 775 780  
 Lys Asp Lys Val Ser Pro Leu Gln Asn Leu Ala Ser Ile Asn Asn Lys  
 785 790 795 800  
 Lys Glu Tyr Ser Asn His Ser Ile Phe Ser Pro Ser Leu Glu Glu Gln  
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 Thr Ala Val Ser Gly Ala Val Asn Asp Ser Ile Lys Ala Ile Ala Ser  
 820 825 830  
 Ile Ala Glu Lys Tyr Phe Gly Ser Thr Gly Leu Val Gly Leu Gln Asp  
 835 840 845  
 Lys Lys Val Gly Ala Leu Pro Tyr Pro Ser Met Phe Pro Leu Pro Phe  
 850 855 860  
 Phe Pro Ala Phe Ser Gln Ser Met Tyr Pro Phe Pro Asp Arg Asp Leu  
 865 870 875 880  
 Arg Ser Leu Pro Leu Lys Met Glu Pro Gln Ser Pro Gly Glu Val Lys  
 885 890 895

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Lys Leu Gln Lys Gly Ser Ser Glu Ser Pro Phe Asp Leu Thr Thr Lys  
 900 905 910  
 Arg Lys Asp Glu Lys Pro Leu Thr Pro Val Pro Ser Lys Pro Pro Val  
 915 920 925  
 Thr Pro Ala Thr Ser Gln Asp Gln Pro Leu Asp Leu Ser Met Gly Ser  
 930 935 940  
 Arg Ser Arg Ala Ser Gly Thr Lys Leu Thr Glu Pro Arg Lys Asn His  
 945 950 955 960  
 Val Phe Gly Gly Lys Lys Gly Ser Asn Val Glu Ser Arg Pro Ala Ser  
 965 970 975  
 Asp Gly Ser Leu Gln His Ala Arg Pro Thr Pro Phe Phe Met Asp Pro  
 980 985 990  
 Ile Tyr Arg Val Glu Lys Arg Lys Leu Thr Asp Pro Leu Glu Ala Leu  
 995 1000 1005  
 Lys Glu Lys Tyr Leu Arg Pro Ser Pro Gly Phe Leu Phe His Pro Gln  
 1010 1015 1020  
 Met Ser Ala Ile Glu Asn Met Ala Glu Lys Leu Glu Ser Phe Ser Ala  
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 Leu Lys Pro Glu Ala Ser Glu Leu Leu Gln Ser Val Pro Ser Met Phe  
 1045 1050 1055  
 Asn Phe Arg Ala Pro Pro Asn Ala Leu Pro Glu Asn Leu Leu Arg Lys  
 1060 1065 1070  
 Gly Lys Glu Arg Tyr Thr Cys Arg Tyr Cys Gly Lys Ile Phe Pro Arg  
 1075 1080 1085  
 Ser Ala Asn Leu Thr Arg His Leu Arg Thr His Thr Gly Glu Gln Pro  
 1090 1095 1100  
 Tyr Arg Cys Lys Tyr Cys Asp Arg Ser Phe Ser Ile Ser Ser Asn Leu  
 1105 1110 1115 1120  
 Gln Arg His Val Arg Asn Ile His Asn Lys Glu Lys Pro Phe Lys Cys  
 1125 1130 1135  
 His Leu Cys Asp Arg Cys Phe Gly Gln Gln Thr Asn Leu Asp Arg His  
 1140 1145 1150  
 Leu Lys Lys His Glu Asn Gly Asn Met Ser Gly Thr Ala Thr Ser Ser  
 1155 1160 1165  
 Pro His Ser Glu Leu Glu Ser Thr Gly Ala Ile Leu Asp Asp Lys Glu  
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 Asp Ala Tyr Phe Thr Glu Ile Arg Asn Phe Ile Gly Asn Ser Asn His  
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 Gly Ser Gln Ser Pro Arg Asn Val Glu Glu Arg Met Asn Gly Ser His



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Phe Lys Asp Glu Lys Ala Leu Val Thr Ser Gln Asn Ser Asp Leu Leu  
1220 1225 1230

Asp Asp Glu Glu Val Glu Asp Glu Val Leu Leu Asp Glu Glu Asp Glu  
1235 1240 1245

Asp Asn Asp Ile Thr Gly Lys Thr Gly Lys Glu Pro Val Thr Ser Asn  
1250 1255 1260

Leu His Glu Gly Asn Pro Glu Asp Asp Tyr Glu Glu Thr Ser Ala Leu  
1265 1270 1275 1280

Glu Met Ser Cys Lys Thr Ser Pro Val Arg Tyr Lys Glu Glu Glu Tyr  
1285 1290 1295

Lys Ser Gly Leu Ser Ala Leu Asp His Ile Arg His Phe Thr Asp Ser  
1300 1305 1310

Leu Lys Met Arg Lys Met Glu Asp Asn Gln Tyr Ser Glu Ala Glu Leu  
1315 1320 1325

Ser Ser Phe Ser Thr Ser His Val Pro Glu Glu Leu Lys Gln Pro Leu  
1330 1335 1340

His Arg Lys Ser Lys Ser Gln Ala Tyr Ala Met Met Leu Ser Leu Ser  
1345 1350 1355 1360

Asp Lys Glu Ser Leu His Ser Thr Ser His Ser Ser Ser Asn Val Trp  
1365 1370 1375

His Ser Met Ala Arg Ala Ala Glu Ser Ser Ala Ile Gln Ser Ile  
1380 1385 1390

Ser His Val  
1395

&lt;210&gt; 106

&lt;211&gt; 5938

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 106

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&lt;210&gt; 107

&lt;211&gt; 261

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 107

Met Asn Pro Ser Arg Asp Val His Asp Ala Ser Thr Ser Arg Arg Phe  
1 5 10 15

Thr Pro Pro Ser Thr Ala Leu Ser Pro Gly Lys Met Ser Glu Ala Leu  
20 25 30

Pro Leu Gly Ala Pro Asp Ala Gly Ala Ala Leu Ala Gly Lys Leu Arg  
35 40 45

Ser Gly Asp Arg Ser Met Val Glu Val Leu Ala Asp His Pro Gly Glu  
50 55 60

Leu Val Arg Thr Asp Ser Pro Asn Phe Leu Cys Ser Val Leu Thr Thr  
65 70 75 80

His Trp Arg Cys Asn Lys Thr Leu Pro Ile Ala Phe Lys Val Val Ala  
85 90 95

Leu Gly Asp Val Pro Asp Gly Thr Leu Val Thr Val Met Ala Gly Asn  
100 105 110

Asp Glu Asn Tyr Ser Ala Glu Leu Arg Asn Ala Thr Ala Ala Met Lys



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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 109

```

tgtcgggtcga agtgggaagag ggaaaaagctt cactctgacc atcactgtct tcacaaaccc 60
accgcaagtc gccacctacc acagagccat caaaatcaca gtggatgggc cccgagaacc 120
tcgaaaaatca tggatgctgc caattttgag cagtttttgc aagaaaggat caaagtgaac 180
ggaaaaagctg ggaaccttgg tggaggggtg gtgacctcgc aaagagagcaa gagcaagatc 240
accgtgacat ccgaggtgcc ttctccaaa aggtatttga aatatctcac caaaaaatat 300
tgaagaaga ataatctacg tgactggttg cgcgtagtgt ctaacagcaa agagagttac 360
gaattacgtt acttccagat taaccaggac gaagaagagg aggaagacga ggattaaatt 420
tcatttatct ggaaaaattt gtatgagttc ttgaataaaa cttgggaacc 470

```

&lt;210&gt; 110

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 110

```

Gly Met Gly Gly Ser Asp Arg Gly Gly Phe Asn Lys Phe Gly Gly Ser
  1             5             10             15

```

Gly

&lt;210&gt; 111

&lt;211&gt; 55

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 111

```

gtggcatggg cggaagtgc cgtggtggct tcaataaatt tggtagcagt ggcca 55

```

&lt;210&gt; 112

&lt;211&gt; 32

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 112

```

Gly Met Gly Arg Trp Lys Leu His Val Leu Ser Ser Asn Leu Ser Ser
  1             5             10             15

```

```

Pro Ala Glu Val Thr Val Val Ala Ser Ile Asn Leu Val Ala Val Ala
      20             25             30

```

&lt;210&gt; 113

&lt;211&gt; 99

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 113

```

gtggcatggg ccgttggag cttcatgtcc ttctctctaa cttgtcttct ccagcgggaag 60
tgaccgtggt ggcttcaata aatttggtag cagtggcca 99

```

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<210> 114  
 <211> 120  
 <212> DNA  
 <213> Homo sapiens

<400> 114  
 atccttttga tcgttggtgc caaggcttgt gtgtgtgtga gtgtgtggga gacaactocg 60  
 aacagtcctg agccctatgt ctttatggct actgggtaaa atagtcaagt gagaatttag 120

<210> 115  
 <211> 375  
 <212> PRT  
 <213> Homo sapiens

<400> 115  
 Met Ser Ala Ser Ala Pro Ala Ala Glu Gly Glu Gly Thr Pro Thr Gln  
 1 5 10 15  
 Pro Ala Ser Glu Lys Glu Pro Glu Met Pro Gly Pro Arg Glu Glu Ser  
 20 25 30  
 Glu Glu Glu Glu Asp Glu Asp Asp Glu Glu Glu Glu Glu Glu Lys  
 35 40 45  
 Glu Lys Ser Leu Ile Val Glu Gly Lys Arg Glu Lys Lys Val Glu  
 50 55 60  
 Arg Leu Thr Met Gln Val Ser Ser Leu Gln Arg Glu Pro Phe Thr Ile  
 65 70 75 80  
 Ala Gln Gly Lys Gly Gln Lys Leu Cys Glu Ile Glu Arg Ile His Phe  
 85 90 95  
 Phe Leu Ser Lys Lys Lys Thr Asp Glu Leu Arg Asn Leu His Lys Leu  
 100 105 110  
 Leu Tyr Asn Arg Pro Gly Thr Val Ser Ser Leu Lys Lys Asn Val Gly  
 115 120 125  
 Gln Phe Ser Gly Phe Pro Phe Glu Lys Gly Ser Val Gln Tyr Lys Lys  
 130 135 140  
 Lys Glu Glu Met Leu Lys Lys Phe Arg Asn Ala Met Leu Lys Ser Ile  
 145 150 155 160  
 Cys Glu Val Leu Asp Leu Glu Arg Ser Gly Val Asn Ser Glu Leu Val  
 165 170 175  
 Lys Arg Ile Leu Asn Phe Leu Met His Pro Lys Pro Ser Gly Lys Pro  
 180 185 190  
 Leu Pro Lys Ser Lys Lys Thr Cys Ser Lys Gly Ser Lys Glu Arg  
 195 200 205  
 Asn Ser Ser Gly Met Ala Arg Lys Ala Lys Arg Thr Lys Cys Pro Glu  
 210 215 220

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```

Ile Leu Ser Asp Glu Ser Ser Asp Glu Asp Glu Lys Lys Asn Lys
225          230          235          240

Glu Glu Ser Ser Asp Asp Glu Asp Lys Glu Ser Glu Glu Glu Pro Pro
          245          250          255

Lys Lys Thr Ala Lys Arg Glu Lys Pro Lys Gln Lys Ala Thr Ser Lys
          260          265          270

Ser Lys Lys Ser Val Lys Ser Ala Asn Val Lys Lys Ala Asp Ser Ser
          275          280          285

Thr Thr Lys Lys Asn Gln Asn Ser Ser Lys Lys Glu Ser Glu Ser Glu
          290          295          300

Asp Ser Ser Asp Asp Glu Pro Leu Ile Lys Lys Leu Lys Lys Pro Pro
305          310          315          320

Thr Asp Glu Glu Leu Lys Glu Thr Ile Lys Lys Leu Leu Ala Ser Ala
          325          330          335

Asn Leu Glu Glu Val Thr Met Lys Gln Ile Cys Lys Lys Val Tyr Glu
          340          345          350

Asn Tyr Pro Thr Tyr Asp Leu Thr Glu Arg Lys Asp Phe Ile Lys Thr
          355          360          365

Thr Val Lys Glu Leu Ile Ser
          370          375

```

&lt;210&gt; 116

&lt;211&gt; 2699

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (1740)

&lt;223&gt; a, c, t, g, other or unknown

&lt;400&gt; 116

```

ggcccgccgc ggccgaaatc cgcgggttcac agcatgtccg cctcgggccc tgctgcccgg 60
ggggaggagaa ccccccacca gcccgcgctcc gagaaaagaac ccgaaatgcc cgggtcccaga 120
gaggagagcgg aggagggaaga ggacgaggac gacgaggagg aggaggagga ggaaaaagaa 180
aagagtctca tcgtggaagg caagagggaa aagaaaaaag tagagaggtt gacaatgcga 240
gtctctctct tacagagaga gccatttaca attgcacaag gaaaggggca gaaactttgt 300
gaaatttgaga ggatacattt tttcttaagt aagaagaaaa cogatgaact tagaaatcta 360
cacaaactcg ttacaacag gccaggcact gtgtcctcat taaagaagaa tgtgggtcag 420
ttcagtggtc ttccatttga aaaaggaagt gtccaatata aaaagaagga agaaatgttg 480
aaaaaattta gaaatgccat gttaaagagc atctgtgagg ttcttgattt ggagagatca 540
gggtgtaata gtgaactagt gaagaggatc ttgaatttct taatgcaccc aaagccttct 600
ggcaaaccat tgcgaaatc taaaaaaact tgtagcaaa gcatgaaaaa ggaacggaac 660
agttctggaa tggcaaggaa ggctaagcga accaaatgtc ctgaaattct gtcagatgaa 720
tctagtatgt atgaagatga aagaaaaaac aagggaagag ctctcagatga tgaagataaa 780
gaaagtgaag aggagccacc aaaaaagaca gccaaaagag aaaaacctaa acagaaagct 840
acttctaaaa gtaaaaaatc tgtgaaaagt gccaatgtta agaaagcaga tagcagcacc 900
accaagaaga atcaaaacag ttccaaaaaa gaaagtgagt ctgaggatag ttcagatgat 960

```

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```

gaaccttttaa ttaaaaagtt gaagaaaccc cctacagatg aagagttaaa ggaacaata 1020
aagaataattac tggccagatgc taacttggaa gaagtacaaa tgaaacagat ttgcataaag 1080
gtctatcgaaa attatcctac ttatgattta actgaaagaa aagatttcat aaaaaaact 1140
gtaaaagagcg taatttcttg agatagagga cagagaagat gactcgttcc catagatttg 1200
aagatctgat ttataccatt ataccagcaa agagaatgta tttccttttc taaatccttg 1260
ttaaagcaacg ttatagaaac ttactgctga cctttttatc ttgagtgtta tgtgaatttg 1320
agtttgcgtg tttaaatgac atttctatgc caatttttag ttataatott goatggcatt 1380
aatgtgtctct tgcttttata gttgtatttt gtacattttg gatttcttta tataagggtca 1440
tagattctctg agctgttttg gtttttagtg cacttaatat tagcttgctt aaggcatact 1500
tttaatacaag tagaacaana actattatca ccaggattta tacatacaga gattgtagta 1560
tttagtatata gaataatttt gaatacacat ctctgtcagt gtgaaaaatc agcggcagtg 1620
tgtccatcat attaaaaata tacaagctac agttgtccag atcactgaat tggaaacttt 1680
ctcctgcagtg tgtatatatg tcaaatgtgc agcatgacaa aagtgcacaga tgttattnn 1740
gtattttttaa aaaaacaattg gttgtatata aagttttttt attctttttg tgcagatcac 1800
tttttaaacat cacataggtta ggtatcttta tagttgtaga ctatggaatg tcatggttca 1860
gccaaacagt atgatggaac agtgaaagtc aattcagtgta tggcaacact gaaggaaacag 1920
ttaccctgat ttgcctcgaa agtgctcatca atttgtaatt ttagatttaa ctctgtaaaa 1980
gtgtctctgag gtactgttta tattatataa ggacagacca aaaaacaccc tatcaagctc 2040
tcaaaaacttg tgggaaaggg tgggattaaag tacaagcaca tttggcttac agtaaatgaa 2100
ctgaattttta ttaactgctt ttgccatat aaaaatgctga tattactgag aaacctagcc 2160
agcttcaaga ttatgactaa agtaccagat tataatgcca gaataataag tgaacgaact 2220
cgtggatgct tctgcacaaag tgtgtctcaa aataatata cttttacatt aaagaaattt 2280
aatgtttctc tggagttggg gctcttggct ttcagagttt gggttaatcag tgttgattct 2340
agatgactcaa cataatggac cactcctgaa tgagacttaa tttgtctttt caaatttact 2400
gtcttaaatc agttttattaa atctgaattt taaaacatgc tgtttatgac acaatgacac 2460
attgtgtgca ccaatttaagt gttgaaaaat atcttggcat catagaacag aaatatataa 2520
aaatatatgt tgaatgttaa caggtatttt ccacaggttg ttcttgata gttactcaga 2580
cactaggggaa aggtaaatca aagtgaacaa aataagcaac taaatgagac ctaataatgt 2640
gccttcgatt ttaaatattt gttcttataa acctgtgcaa taaaataaa tctaaatca 2699

```

<210> 117  
 <211> 288  
 <212> DNA  
 <213> Homo sapiens

```

<400> 117
gtcaacagtc gccaaaatt taaataaaat tattgcagcg ctataataag ttaaatagct 60
aaaatttttaa ataatgcagc attcagtttt tagtgctgac agtgttcttt gatttttgcaa 120
acaaatgagt atttctcaa tgggaagacg tcttatatgt tctatgctgt gaatagatag 180
gtttagaatt cctttcagca cagttttgtc tcaattacag ttaattttat ggggtgggaga 240
gcaaaatctca aatggatgca ctgtctgagt accagaatga atggaaaa 288

```

<210> 118  
 <211> 277  
 <212> PRT  
 <213> Homo sapiens

```

<400> 118
Met Ser Ala Gln Ala Ala Lys Val Ser Lys Lys Glu Leu Asn Ser Asn
1 5 10 15
His Asp Gly Ala Asp Glu Thr Ser Glu Lys Glu Gln Gln Glu Ala Ile
20 25 30
Glu His Ile Asp Glu Val Gln Asn Glu Ile Asp Arg Leu Asn Glu Gln
35 40 45

```



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Ala Ser Glu Glu Ile Leu Lys Val Glu Gln Lys Tyr Asn Lys Leu Arg  
50 55 60

Gln Pro Phe Phe Gln Lys Arg Ser Glu Leu Ile Ala Lys Ile Pro Asn  
65 70 75 80

Phe Trp Val Thr Thr Phe Val Asn His Pro Gln Val Ser Ala Leu Leu  
85 90 95

Gly Glu Glu Asp Glu Glu Ala Leu His Tyr Leu Thr Arg Val Glu Val  
100 105 110

Thr Glu Phe Glu Asp Ile Lys Ser Gly Tyr Arg Ile Asp Phe Tyr Phe  
115 120 125

Asp Glu Asn Pro Tyr Phe Glu Asn Lys Val Leu Ser Lys Glu Phe His  
130 135 140

Leu Asn Glu Ser Gly Asp Pro Ser Ser Lys Ser Thr Glu Ile Lys Trp  
145 150 155 160

Lys Ser Gly Lys Asp Leu Thr Lys Arg Ser Ser Gln Thr Gln Asn Lys  
165 170 175

Ala Ser Arg Lys Arg Gln His Glu Glu Pro Glu Ser Phe Phe Thr Trp  
180 185 190

Phe Thr Asp His Ser Asp Ala Gly Ala Asp Glu Leu Gly Glu Val Ile  
195 200 205

Lys Asp Asp Ile Trp Pro Asn Pro Leu Gln Tyr Tyr Leu Val Pro Asp  
210 215 220

Met Asp Asp Glu Glu Gly Glu Gly Glu Asp Asp Asp Asp Glu  
225 230 235 240

Glu Glu Glu Gly Leu Glu Asp Ile Asp Glu Glu Gly Asp Glu Asp Glu  
245 250 255

Gly Glu Glu Asp Glu Asp Asp Asp Glu Gly Glu Glu Gly Glu Glu Asp  
260 265 270

Glu Gly Glu Asp Asp  
275

&lt;210&gt; 119

&lt;211&gt; 2577

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 119

cacatgtcgg cgcaggcggc caaagtcagt aaaaaggagc tcaactccaa ccacgacggg 60  
gccgacgaga cctcagaaaa agaacagcaa gaagcgattg aacacattga tgaagtacaa 120  
aatgaaatag acagacttaa tgaacaagcc agtgaggaga ttttgaaagt agaacagaaa 180  
tataacaaac tccgccaaac attttttcag aagagggtcag aattgatcgc caaaatccca 240  
aatttttggg taacaacatt tgtcaaccat ccacaagtgt ctgcactgct tggggaggaa 300

```

gatgaagagg cactgcatta ttgaccaga gttgaagtga cagaatttga agatattaaa 360
tcaggttaca gaatagattt ttattttgat gaaaatcctt accttgaanaa taaagtcttc 420
tccaaagaat ttcatctgaa tgagagtggt gatccatctt cgaagtcacc cgaatacaaa 480
tggaatcttg gaaaggaattt gacgaaacct tcgagtcaaa cgcagaataa agccagcagg 540
aagaggcagc atgagggaacc agagagcttc ttacctgggt ttactgacca ttctgatgca 600
gggtgctgatg ccgttaggaga gggtcatcaa gatgatattt ggccaaaccc attacagtac 660
tacttggcttc cggatatgga tgatgaagaa ggagaaggag aagaagatga tgatgatgat 720
gaagaggagg aaggattaga agatattgac gaagaagggg atgaggatga aggtgaagaa 780
gatgaagatg atgatgaagg ggagggaagga gaggaggatg aaggagaaga tgactaaata 840
gaacactgat ggattccaac ctctcctttt taaattttt ctcagtcctc gggagcagg 900
tgcagtcctt ttcttttttt cctctctgtg ctcagtcgcc ttcttcttga 960
gggtctcttt ctctactcca tgggtctcaa ttattttggg gggaaatacc ttgagcagaa 1020
tacaatggga aaagagcttc taccctcttc tgttcgaagt tcatttttat cctctcctgt 1080
ctgaacaaaa actgtatgga atcaacacca ccgagctctg tgggaaaaaa gaaaaacctg 1140
ctcccttttg ctctgtggaa gctggagggt gctaggcccc tgtgtagtag tgtatagaat 1200
ctctagcttt ttctctcttt ctctgtatat tgggctcaga gagtacactg tgtctctatg 1260
tgaatatgga cagttagcat ttaccaacat gatatctgtc accttctctt tgttaaaaaa 1320
agaaaaaaaa acttaaaaaa atggggttat agaaagtcag caaagggctg gggtttgaga 1380
tggttgggtg ggttagtggt catttttgaca acatggcttc tctcttggca tggtttaatt 1440
tgatatgga cggacatcct tgcagtttaa gatgacactt ttaaaataaa ttctctctta 1500
atgatgactt gagccctgcc actcaatggg agaactcagc gaacctgtag gatcttattt 1560
ggaattgaca ttctctattg taattttgtt cctgtttatt ttggggttct tttttgttct 1620
actggaaagg aaagatgatg ctacagttta aacgttaaaa gtgtacaagt tggtttgata 1680
caataaaact aaatgtgtac acaaggattt tgatgctttt ctctcagcat aggtatgctt 1740
actatgacct tccaagtttg actcactgtc caactttgtc aaacttttgc accttaattt 1800
cgtatttttt gatcagcact ttgtcaggat gacctcaggg ctatgtggat tgagtaattg 1860
gattgaaatc atgtatttaa tatctccata gctgggaaac gtgggttcaa ttgtccattg 1920
gtttctgaaa agtattcaca ctattttgga taccagatag ctcaatactc tctgagtaca 1980
ttgtgcctct gatittttatc tccaagtggc agtttttaaa attggccttt taactggata 2040
taaatatttt gtgcctgccca ccaccatcca acagacctgg tgcctctaag ccaagtata 2100
cacgggacag ttgtcggcat gtcttcattg gctctctaaa atgtggccaa gaagataggc 2160
tctcagtaag aagctctgat gtgagcagta actgtccctg ctctctggta taaagctctc 2220
aaatgtgacc atgtgaatct ggggtgggata atggactcag ctctgtctcg tcaatgccat 2280
tggtcagaga agcacctcaa tgcataagct tttaaatgct gtaaaatata tgcgtcgaaa 2340
ttaaagccca ctttttcaga ggtgaattaa tggcagctct ggtgaacttc aaaagctttt 2400
tgatgtataa aacttgataa atggaactat tccatcaata ggcaaaagtg taacaaccta 2460
tctagatgga tagtatgtaa ttcttcgaca ggtctctggt tagtaataac atcactgat 2520
accgatcagg aatcttgcct caataaagga acataaagat ttaaaaaaaa aaaaaa 2577

```

&lt;210&gt; 120

&lt;211&gt; 288

&lt;212&gt; FRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 120

Ala Leu Ser Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser  
 1 5 10 15

Thr Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln  
 20 25 30

Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg  
 35 40 45

Met Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys  
 50 55 60

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His Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu  
 65 70 75 80  
 Asn Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile  
 85 90 95  
 Ser Asn Ile Asn Val Ile Val Leu Glu Leu Lys Met Ala Gly Gln Cys  
 100 105 110  
 Ser Gln Asn Glu Tyr Phe Asp Ser Leu Leu His Ala Cys Ile Pro Cys  
 115 120 125  
 Gln Leu Arg Cys Ser Ser Asn Thr Pro Pro Leu Thr Cys Gln Arg Tyr  
 130 135 140  
 Cys Asn Ala Ser Val Thr Asn Ser Val Lys Gly Thr Asn Ala Ile Leu  
 145 150 155 160  
 Trp Thr Cys Leu Gly Leu Ser Leu Ile Ile Ser Leu Ala Val Phe Val  
 165 170 175  
 Leu Met Phe Leu Leu Arg Lys Ile Ser Ser Glu Pro Leu Lys Asp Glu  
 180 185 190  
 Phe Lys Asn Thr Gly Ser Gly Leu Leu Gly Met Ala Asn Ile Asp Leu  
 195 200 205  
 Glu Lys Ser Arg Thr Gly Asp Glu Ile Ile Leu Pro Arg Gly Leu Glu  
 210 215 220  
 Tyr Thr Val Glu Glu Cys Thr Cys Glu Asp Cys Ile Lys Ser Lys Pro  
 225 230 235 240  
 Lys Val Asp Ser Asp His Cys Phe Pro Leu Pro Ala Met Glu Glu Gly  
 245 250 255  
 Ala Thr Ile Leu Val Thr Thr Lys Thr Asn Asp Tyr Cys Lys Ser Leu  
 260 265 270  
 Pro Ala Ala Leu Ser Ala Thr Glu Ile Glu Lys Ser Ile Ser Ala Arg  
 275 280 285

&lt;210&gt; 121

&lt;211&gt; 1073

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 121

gcactaagtc ttgcacttgt cacaaacagt gcacctactt caagttctac aaagaaaaca 60  
 cagctacaac tggagcatatt actgctggat ttacagatga ttttgaatgg aattaataat 120  
 tacaagaatc ccaactcac caggatgctc acatttaagt tttacatgcc caagaaggcc 180  
 acagaactga aacatcttca gtgtctagaa gaagaactca aacctctgga ggaagtgtca 240  
 aatttagctc aaagcaaaaa ctttcaactta agacccaggg acttaatcag caatatacac 300  
 gtaatatgtc tggaaactaaa gatggctggg cagtgctccc aaaatgaata ttttgacagt 360  
 ttgtttgcag cttgcatacc ttgtcaactt cgaatgttctt ctaatactcc tctctcaaca 420  
 tgtcagcgtt attgtaatgc aagtgtgacc aattcagtg aaggaaacaa tgcgattctc 480  
 tggacctggt tgggaactgag cttaataatt tctttggcag ttttcgtgct aatgtttttg 540

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```

ctaaggaaga taagctctga accattaaag gacgagttta aaaacacagg atcagggtctc 600
ctgggcatgg ctaacattga cctggaaaag agcaggactg gtgatgaaat tattcttccg 660
agaggcctcg agtacacggg ggaagaatgc acctgtgaag actgcatcaa gagcaaacgg 720
aaggctgact ctgaccattg ctttccactc ccagctatgg aggaaggcgc aaccattctt 780
gtcaccacga aaacgaatga ctattgcaag agcctgccag ctgcttttag tgctacggag 840
atagagaaat caatttctgc taggtaatta accatttctg ctcgagcagt gccactttaa 900
aaatcttttg tcagaaataga tgatgtgtca gatctcttta ggatgactgt atttttcagt 960
tgccgataca gctttttgtc ctctaactgt ggaactctt tatgttagat atatttctct 1020
aggttactgt tgggagctta atggtagaaa cttccttggt ttctatgatt aaa 1073

```

&lt;210&gt; 122

&lt;211&gt; 26

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 122

```

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Phe Lys
  1             5             10             15

```

Arg Ala Lys Ala Asn Leu Asp Lys Asn Lys

20

25

&lt;210&gt; 123

&lt;211&gt; 78

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 123

```

gaatttgaag atagagacag gtctcatcgg gaggaatagg agttcaagag ggccaaggcg 60
aacctagaca agaataag
                                     78

```

&lt;210&gt; 124

&lt;211&gt; 34

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 124

```

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Val His
  1             5             10             15

```

Glu Leu Glu Lys Ser Lys Arg Ala Leu Glu Thr Gln Met Glu Glu Met

20

25

30

Lys Thr

&lt;210&gt; 125

&lt;211&gt; 102

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 125

```

gaatttgaag atagagacag gtctcatcgg gaggaatagg aggtccatga gctggagaag 60
tccaagcggg ccttgagac ccagatggag gagatgaaga cg 102

```

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&lt;210&gt; 126

&lt;211&gt; 50

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 126

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Asn Glu  
1 5 10 15

Val Glu Ser Val Thr Gly Met Leu Asn Glu Ala Glu Gly Lys Ala Ile  
20 25 30

Lys Leu Ala Lys Asp Val Ala Ser Leu Ser Ser Gln Leu Gln Asp Thr  
35 40 45

Gln Glu  
50

&lt;210&gt; 127

&lt;211&gt; 152

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 127

gaatttgaag atagagacag gtctcatcgg gaggaatgg agaatgaagt tgagagcgctc 60  
acaggggatgc ttaacgagggc cgagggggaag gccattaagc tggccaagga cgtggcgctcc 120  
ctcaggtccc agctccagga caccaggag tt 152

&lt;210&gt; 128

&lt;211&gt; 1353

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (941)

&lt;223&gt; a, c, t, g, other or unknown

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (1067)

&lt;223&gt; a, c, t, g, other or unknown

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (1077)

&lt;223&gt; a, c, t, g, other or unknown

&lt;400&gt; 128

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taccataagg ggtttaaata ggaatgtttt ctccaaagtg aatcttgaaa tcttggtgtt 180  
tataattgtc aagcctcttt ttttaaaata gatttggtea acaggaagta tttttttcta 240  
atttttattt tatagaccta gtcaagcttc ttaattgtta aatattgtta taacaataca 300  
tctgggcggg gcgcgggtggc tcactcctgt aatcccagca ctttgggagg ccagggcgagg 360

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gaggcgggagc ttgcgggtgag ccaagatcgc gccactgcac tccagcgact ccgtctcaaa 540
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&lt;210&gt; 129

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (326)

&lt;223&gt; a, c, t, g, other or unknown

&lt;220&gt;

&lt;221&gt; modified\_base

&lt;222&gt; (614)

&lt;223&gt; a, c, t, g, other or unknown

&lt;400&gt; 129

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gaaaattggg gatatatgt gatacttgtt ttctttgatg ctgttgtaat tctttgtatt 180
tctatatatg tgaatacaag acttccacac catgcccttt ctcttcgtaat tctgtaaaatt 240
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cgggctggaa gtcaacatgc aggcgctcaa gggccagttc gaaaggagtc tccaaagccg 720
ggacgagcag aatgaggaga agag

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&lt;210&gt; 130

&lt;211&gt; 29

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 130

Arg Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Glu

1

5

10

15

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Leu Leu Gln Glu Glu Thr Arg Gln Lys Leu Asn Val Ser  
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 <212> DNA  
 <213> Homo sapiens

<400> 131  
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 agaaaccggg cagaagctca acgtgtcta 89

<210> 132  
 <211> 452  
 <212> PRT  
 <213> Homo sapiens

<400> 132  
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 20 25 30  
 Leu His Val Pro Val Pro Arg Ala Leu Arg Met Glu Glu Asp Ser Ile  
 35 40 45  
 Arg Leu Pro Ala His Leu Arg Leu Gln Pro Ile Tyr Trp Ser Arg Asp  
 50 55 60  
 Asp Val Ala Gln Trp Leu Lys Trp Ala Glu Asn Glu Phe Ser Leu Arg  
 65 70 75 80  
 Pro Ile Asp Ser Asn Thr Phe Glu Met Asn Gly Lys Ala Leu Leu Leu  
 85 90 95  
 Leu Thr Lys Glu Asp Phe Arg Tyr Arg Ser Pro His Ser Gly Asp Val  
 100 105 110  
 Leu Tyr Glu Leu Leu Gln His Ile Leu Lys Gln Arg Lys Pro Arg Ile  
 115 120 125  
 Leu Phe Ser Pro Phe Phe His Pro Gly Asn Ser Ile His Thr Gln Pro  
 130 135 140  
 Glu Val Ile Leu His Gln Asn His Glu Glu Asp Asn Cys Val Gln Arg  
 145 150 155 160  
 Thr Pro Arg Pro Ser Val Asp Asn Val His His Asn Pro Pro Thr Ile  
 165 170 175  
 Glu Leu Leu His Arg Ser Arg Ser Pro Ile Thr Thr Asn His Arg Pro  
 180 185 190  
 Ser Pro Asp Pro Glu Gln Arg Pro Leu Arg Ser Pro Leu Asp Asn Met

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195                      200                      205  
 Ile Arg Arg Leu Ser Pro Ala Glu Arg Ala Gln Gly Pro Arg Pro His  
     210                      215                      220  
 Gln Glu Asn Asn His Gln Glu Ser Tyr Pro Leu Ser Val Ser Pro Met  
     225                      230                      235                      240  
 Glu Asn Asn His Cys Pro Ala Ser Ser Glu Ser His Pro Lys Pro Ser  
                          245                      250                      255  
 Ser Pro Arg Gln Glu Ser Thr Arg Val Ile Gln Leu Met Pro Ser Pro  
     260                      265                      270  
 Ile Met His Pro Leu Ile Leu Asn Pro Arg His Ser Val Asp Phe Lys  
     275                      280                      285  
 Gln Ser Arg Leu Ser Glu Asp Gly Leu His Arg Glu Gly Lys Pro Ile  
     290                      295                      300  
 Asn Leu Ser His Arg Glu Asp Leu Ala Tyr Met Asn His Ile Met Val  
     305                      310                      315                      320  
 Ser Val Ser Pro Pro Glu Glu His Ala Met Pro Ile Gly Arg Ile Ala  
                          325                      330                      335  
 Asp Cys Arg Leu Leu Trp Asp Tyr Val Tyr Gln Leu Leu Ser Asp Ser  
     340                      345                      350  
 Arg Tyr Glu Asn Phe Ile Arg Trp Glu Asp Lys Glu Ser Lys Ile Phe  
     355                      360                      365  
 Arg Ile Val Asp Pro Asn Gly Leu Ala Arg Leu Trp Gly Asn His Lys  
     370                      375                      380  
 Asn Arg Thr Asn Met Thr Tyr Glu Lys Met Ser Arg Ala Leu Arg His  
     385                      390                      395                      400  
 Tyr Tyr Lys Leu Asn Ile Ile Arg Lys Glu Pro Gly Gln Arg Leu Leu  
     405                      410                      415  
 Phe Arg Phe Met Lys Thr Pro Asp Glu Ile Met Ser Gly Arg Thr Asp  
     420                      425                      430  
 Arg Leu Glu His Leu Glu Ser Gln Glu Leu Asp Glu Gln Ile Tyr Gln  
     435                      440                      445  
 Glu Asp Glu Cys  
     450

&lt;210&gt; 133

&lt;211&gt; 1956

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 133

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tctctgacc ccgagcagcg gccctccogg tccccctcgg acaacatgat ccgcccgttc 660
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tccgaggagc ggcgtcatag ggaagggaag cccatcaacc tctctcatcg ggaagacctg 960
gcttacatga accacatcat ggtctctgtc tccccgctg aagagcacgc catgcccatt 1020
gggagaatag cagactgtag actgctttgg gattacgtct atcagttgct tctgacagc 1080
cggtacgaaa acttcatccg atgggaggac aaagaatcca aaatattccg gatagtggt 1140
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aaaatgtcca gaccctcgcg ccaactactc aaactaaaac ttatcaggaa ggacccaggga 1260
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tactgttggt tcttggtcga aaaaaaaaa aaaaaa 1956

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&lt;210&gt; 134

&lt;211&gt; 452

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 134

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Met Ser Glu Thr Pro Ala Gln Cys Ser Ile Lys Gln Glu Arg Ile Ser
  1             5             10             15

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Tyr Thr Pro Pro Glu Ser Pro Val Pro Ser Tyr Ala Ser Ser Thr Pro
      20             25             30

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Leu His Val Pro Val Pro Arg Ala Leu Arg Met Glu Glu Asp Ser Ile
      35             40             45

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Arg Leu Pro Ala His Leu Arg Leu Gln Pro Ile Tyr Trp Ser Arg Asp
      50             55             60

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Asp Val Ala Gln Trp Leu Lys Trp Ala Glu Asn Glu Phe Ser Leu Arg
      65             70             75             80

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Pro Ile Asp Ser Asn Thr Phe Glu Met Asn Gly Lys Ala Leu Leu Leu
      85             90             95

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Leu Thr Lys Glu Asp Phe Arg Tyr Arg Ser Pro His Ser Gly Asp Val  
 100 105 110  
 Leu Tyr Glu Leu Leu Gln His Ile Leu Lys Gln Arg Lys Pro Arg Ile  
 115 120 125  
 Leu Phe Ser Pro Phe Phe His Pro Gly Asn Ser Ile His Thr Gln Pro  
 130 135 140  
 Glu Val Ile Leu His Gln Asn His Glu Glu Asp Asn Cys Val Gln Arg  
 145 150 155 160  
 Thr Pro Arg Pro Ser Val Asp Asn Val His Asn Pro Pro Thr Ile  
 165 170 175  
 Glu Leu Leu His Arg Ser Arg Ser Pro Ile Thr Thr Asn His Arg Pro  
 180 185 190  
 Ser Pro Asp Pro Glu Gln Arg Pro Leu Arg Ser Pro Leu Asp Asn Met  
 195 200 205  
 Ile Arg Arg Leu Ser Pro Ala Glu Arg Ala Gln Gly Pro Arg Pro His  
 210 215 220  
 Gln Glu Asn Asn His Gln Glu Ser Tyr Pro Leu Ser Val Ser Pro Met  
 225 230 235 240  
 Glu Asn Asn His Cys Pro Ala Ser Ser Glu Ser His Pro Lys Pro Ser  
 245 250 255  
 Ser Pro Arg Gln Glu Ser Thr Arg Val Ile Gln Leu Met Pro Ser Pro  
 260 265 270  
 Ile Met His Pro Leu Ile Leu Asn Pro Arg His Ser Val Asp Phe Lys  
 275 280 285  
 Gln Ser Arg Leu Ser Glu Asp Gly Leu His Arg Glu Gly Lys Pro Ile  
 290 295 300  
 Asn Leu Ser His Arg Glu Asp Leu Ala Tyr Met Asn His Ile Met Val  
 305 310 315 320  
 Ser Val Ser Pro Pro Glu Glu His Ala Met Pro Ile Gly Arg Ile Ala  
 325 330 335  
 Asp Cys Arg Leu Leu Trp Asp Tyr Val Tyr Gln Leu Leu Ser Asp Ser  
 340 345 350  
 Arg Tyr Glu Asn Phe Ile Arg Trp Glu Asp Lys Glu Ser Lys Ile Phe  
 355 360 365  
 Arg Ile Val Asp Pro Asn Gly Leu Ala Arg Leu Trp Gly Asn His Lys  
 370 375 380  
 Asn Arg Thr Asn Met Thr Tyr Glu Lys Met Ser Arg Ala Leu Arg His  
 385 390 395 400  
 Tyr Tyr Lys Leu Asn Ile Ile Arg Lys Glu Pro Gly Gln Arg Leu Leu

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405

410

415

Phe Arg Phe Met Lys Thr Pro Asp Glu Ile Met Ser Gly Arg Thr Asp  
 420 425 430

Arg Leu Glu His Leu Glu Ser Gln Glu Leu Asp Glu Gln Ile Tyr Gln  
 435 440 445

Glu Asp Glu Cys  
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&lt;210&gt; 135

&lt;211&gt; 1580

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 135

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&lt;210&gt; 136

&lt;211&gt; 1451

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 136

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<210> 137  
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 <212> DNA  
 <213> Homo sapiens

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<400> 137
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agtttgcctc ctttagtgca gttgcttggt tccagtttg gacttaaagg atgggtatag 180
tactactgtc tttttaatag gttccaatgt gactctagaa attggagagg acaaatataa 240
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gaagggggtt cgtgatgttg gccaggccga tcttgaaact ctggccttaa gctgatctgc 480
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&lt;210&gt; 138

110/299

&lt;211&gt; 1679

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 138

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&lt;210&gt; 139

&lt;211&gt; 680

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 139

```

Met Glu Asp Ser Met Asp Met Ser Pro Leu Arg Pro Gln Asn
  1             5             10             15

Tyr Leu Phe Gly Cys Glu Leu Lys Ala Asp Lys Asp Tyr His Phe Lys
    20             25             30

Val Asp Asn Asp Glu Asn Glu His Gln Leu Ser Leu Arg Thr Val Ser
    35             40             45

Leu Gly Ala Gly Ala Lys Asp Glu Leu His Ile Val Glu Ala Glu Ala
    50             55             60

Met Asn Tyr Glu Gly Ser Pro Ile Lys Val Thr Leu Ala Thr Leu Lys
    65             70             75             80

Met Ser Val Gln Pro Thr Val Ser Leu Gly Gly Phe Glu Ile Thr Pro
    85             90             95

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Pro Val Val Leu Arg Leu Lys Cys Gly Ser Gly Pro Val His Ile Ser  
 100 105 110  
 Gly Gln His Leu Val Val Tyr Arg Arg Lys His Gln Glu Leu Gln Ala  
 115 120 125  
 Met Gln Met Glu Leu Gln Ser Pro Glu Tyr Lys Leu Ser Lys Leu Arg  
 130 135 140  
 Thr Ser Thr Ile Met Thr Asp Tyr Asn Pro Asn Tyr Cys Phe Ala Gly  
 145 150 155 160  
 Lys Thr Ser Ser Ile Ser Asp Leu Lys Glu Val Pro Arg Lys Asn Ile  
 165 170 175  
 Thr Leu Ile Arg Gly Leu Gly His Gly Ala Phe Gly Glu Val Tyr Glu  
 180 185 190  
 Gly Gln Val Ser Gly Met Pro Asn Asp Pro Ser Pro Leu Gln Val Ala  
 195 200 205  
 Val Lys Thr Leu Pro Glu Val Cys Ser Glu Gln Asp Glu Leu Asp Phe  
 210 215 220  
 Leu Met Glu Ala Leu Ile Ile Ser Lys Phe Asn His Gln Asn Ile Val  
 225 230 235 240  
 Arg Cys Ile Gly Val Ser Leu Gln Ser Leu Pro Arg Phe Ile Leu Leu  
 245 250 255  
 Glu Leu Met Ala Gly Gly Asp Leu Lys Ser Phe Leu Arg Glu Thr Arg  
 260 265 270  
 Pro Arg Pro Ser Gln Pro Ser Ser Leu Ala Met Leu Asp Leu Leu His  
 275 280 285  
 Val Ala Arg Asp Ile Ala Cys Gly Cys Gln Tyr Leu Glu Glu Asn His  
 290 295 300  
 Phe Ile His Arg Asp Ile Ala Ala Arg Asn Cys Leu Leu Thr Cys Pro  
 305 310 315 320  
 Gly Pro Gly Arg Val Ala Lys Ile Gly Asp Phe Gly Met Ala Arg Asp  
 325 330 335  
 Ile Tyr Arg Ala Ser Tyr Tyr Arg Lys Gly Gly Cys Ala Met Leu Pro  
 340 345 350  
 Val Lys Trp Met Pro Pro Glu Ala Phe Met Glu Gly Ile Phe Thr Ser  
 355 360 365  
 Lys Thr Asp Thr Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Ser  
 370 375 380  
 Leu Gly Tyr Met Pro Tyr Pro Ser Lys Ser Asn Gln Glu Val Leu Glu  
 385 390 395 400

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Phe Val Thr Ser Gly Gly Arg Met Asp Pro Pro Lys Asn Cys Pro Gly  
 405 410 415  
 Pro Val Tyr Arg Ile Met Thr Gln Cys Trp Gln His Gln Pro Glu Asp  
 420 425 430  
 Arg Pro Asn Phe Ala Ile Ile Leu Glu Arg Ile Glu Tyr Cys Thr Gln  
 435 440 445  
 Asp Pro Asp Val Ile Asn Thr Ala Leu Pro Ile Glu Tyr Gly Pro Leu  
 450 455 460  
 Val Glu Glu Glu Glu Lys Val Pro Val Arg Pro Lys Asp Pro Glu Gly  
 465 470 475 480  
 Val Pro Pro Leu Leu Val Ser Gln Gln Ala Lys Arg Glu Glu Glu Arg  
 485 490 495  
 Ser Pro Ala Ala Pro Pro Pro Leu Pro Thr Thr Ser Ser Gly Lys Ala  
 500 505 510  
 Ala Lys Lys Pro Thr Ala Ala Glu Val Ser Val Arg Val Pro Arg Gly  
 515 520 525  
 Pro Ala Val Glu Gly Gly His Val Asn Met Ala Phe Ser Gln Ser Asn  
 530 535 540  
 Pro Pro Ser Glu Leu His Lys Val His Gly Ser Arg Asn Lys Pro Thr  
 545 550 555 560  
 Ser Leu Trp Asn Pro Thr Tyr Gly Ser Trp Phe Thr Glu Lys Pro Thr  
 565 570 575  
 Lys Lys Asn Asn Pro Ile Ala Lys Lys Glu Pro His Asp Arg Gly Asn  
 580 585 590  
 Leu Gly Leu Glu Gly Ser Cys Thr Val Pro Pro Asn Val Ala Thr Gly  
 595 600 605  
 Arg Leu Pro Gly Ala Ser Leu Leu Leu Glu Pro Ser Ser Leu Thr Ala  
 610 615 620  
 Asn Met Lys Glu Val Pro Leu Phe Arg Leu Arg His Phe Pro Cys Gly  
 625 630 635 640  
 Asn Val Asn Tyr Gly Tyr Gln Gln Gln Gly Leu Pro Leu Glu Ala Ala  
 645 650 655  
 Thr Ala Pro Gly Ala Gly His Tyr Glu Asp Thr Ile Leu Lys Ser Lys  
 660 665 670  
 Asn Ser Met Asn Gln Pro Gly Pro  
 675 680

&lt;210&gt; 140

&lt;211&gt; 2043

&lt;212&gt; DNA

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&lt;213&gt; Homo sapiens

&lt;400&gt; 140

```

atggaagatt cgatggacat ggacatgagc cccctgaggg cccagaacta tcttttcggt 60
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cagttatctt taagaacgggt cagttatgag gctgggtgcaa aggatgagtt gcacattggt 180
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aggttgaagt gtggttcagg gccagtgcat attagtggac agcacttagt agtgtaaccg 360
cggaagcacc aggagctgca agccatgcag atggagctgc agagccctga gtacaagctg 420
agcaagctcc gcacctcgac catcatgacc gactacaacc ccaactactg ctttctgtgc 480
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gaactggatt tcctcatgga agccctgatc atcagcaaat tcaaccacca gaacattggt 720
cgctgcattg ggggtgagcct gcaatccctg ccccggttca tcctgtgga gctcatggcg 780
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gctggtcatt acgaggatcc cattctgaaa agcaagaata gcatgaacca gctggggccc 2040
tga
2043

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&lt;210&gt; 141

&lt;211&gt; 180

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 141

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caggaccacc ccagtagcat ggggtgttat gggcaggagt ctggaggatt ttccggacca 60
ggagagaacc ggagcatgag tggccctgca tggaggacac ataaagggtt cctggagggt 120
gacaatcaca gttacctctc catactcaca tgaaggagc aggaacttgt ttctattac 180

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&lt;210&gt; 142

&lt;211&gt; 180

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 142

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aagggtgtat attgaggaaa tttagcagg ctgcctgaa gaaaggcata gtgacaagat 60

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gagagagatg cattgttttg agatgtgttt agccagtgcc cttcttcccc acgcatcagg 120  
 tcctggagct taggatgtgt gatgcagaag aagtcctgga aggtaagaaa cagaattgta 180

<210> 143  
 <211> 427  
 <212> DNA  
 <213> Homo sapiens

<400> 143  
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 ctcaactctgc cttcacagtc agcagccact ctctcagagc tgggtgtggga atccaaagt 120  
 aataaatcag agccctcaag acactgaatg ccaggagcat ggtctgaggg acagtgtgct 180  
 ataatagaga tacatatgga ggaagcggag gaggaaggag cagattgtgt ttgagaatgg 240  
 cttaaacaga gttgaagcta tttctcaggg ttatcaactt ccaccagagg aactggaatt 300  
 tgttgtattt ctctcaaaat attgatgggt aacatttatg tttagaatc tcctcttagt 360  
 gcctttacat tactaaacat taagagatga ttgaagggaa aatgcacttt agaccagggt 420  
 aaattag 427

<210> 144  
 <211> 438  
 <212> DNA  
 <213> Homo sapiens

<400> 144  
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 aggaatatgtc agcactgccc tgaacaaat caggcgtggc ccttgccgag cactctggcac 120  
 atagtaggtg ctaaatataat atttgttgaa tggatgaatt gttaggtaag tagaataaga 180  
 gagataggtg ggtaggtagg taggtaggtg ggtagataga tagagacaga taaataaatg 240  
 ggttgacaga tgtgtggaat ggtatgagtg atgggtgagt tgggtggatg atggattgga 300  
 ttgtatagat gaattgaatg gatggttgaa tggatggata gatggatgga tgggtggaat 360  
 agatggatgg acggatggat ggtatggatg atggatggat ggtatggatg tgkatggatg 420  
 gacggacaga cggacgga 438

<210> 145  
 <211> 135  
 <212> DNA  
 <213> Homo sapiens

<400> 145  
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 tacctcttcg gatga 135

<210> 146  
 <211> 476  
 <212> PRT  
 <213> Homo sapiens

<400> 146  
 Met Ala Ser Thr Asp Tyr Ser Thr Tyr Ser Gln Ala Ala Ala Gln Gln  
 1 5 10 15

Gly Tyr Ser Ala Tyr Thr Ala Gln Pro Thr Gln Gly Tyr Ala Gln Thr  
 20 25 30

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Thr Gln Ala Tyr Gly Gln Gln Ser Tyr Gly Thr Tyr Gly Gln Pro Thr  
 35 40 45  
 Asp Val Ser Tyr Thr Gln Ala Gln Thr Thr Ala Thr Tyr Gly Gln Thr  
 50 55 60  
 Ala Tyr Ala Thr Ser Tyr Gly Gln Pro Pro Thr Gly Tyr Thr Thr Pro  
 65 70 75 80  
 Thr Ala Pro Gln Ala Tyr Ser Gln Pro Val Gln Gly Tyr Gly Thr Gly  
 85 90 95  
 Ala Tyr Asp Thr Thr Thr Ala Thr Val Thr Thr Thr Gln Ala Ser Tyr  
 100 105 110  
 Ala Ala Gln Ser Ala Tyr Gly Thr Gln Pro Ala Tyr Pro Ala Tyr Gly  
 115 120 125  
 Gln Gln Pro Ala Ala Thr Ala Pro Thr Arg Pro Gln Asp Gly Asn Lys  
 130 135 140  
 Pro Thr Glu Thr Ser Gln Pro Gln Ser Ser Thr Gly Gly Tyr Asn Gln  
 145 150 155 160  
 Pro Ser Leu Gly Tyr Gly Gln Ser Asn Tyr Ser Tyr Pro Gln Val Pro  
 165 170 175  
 Gly Ser Tyr Pro Met Gln Pro Val Thr Ala Pro Pro Ser Tyr Pro Pro  
 180 185 190  
 Thr Ser Tyr Ser Ser Thr Gln Pro Thr Ser Tyr Asp Gln Ser Ser Tyr  
 195 200 205  
 Ser Gln Gln Asn Thr Tyr Gly Gln Pro Ser Ser Tyr Gly Gln Gln Ser  
 210 215 220  
 Ser Tyr Gly Gln Gln Ser Ser Tyr Gly Gln Gln Pro Pro Thr Ser Tyr  
 225 230 235 240  
 Pro Pro Gln Thr Gly Ser Tyr Ser Gln Ala Pro Ser Gln Tyr Ser Gln  
 245 250 255  
 Gln Ser Ser Ser Tyr Gly Gln Gln Ser Pro Pro Leu Gly Gly Ala Gln  
 260 265 270  
 Thr Ile Ser Lys Asn Thr Glu Gln Arg Pro Gln Pro Asp Pro Tyr Gln  
 275 280 285  
 Ile Leu Gly Pro Thr Ser Ser Arg Leu Ala Asn Pro Gly Ser Gly Gln  
 290 295 300  
 Ile Gln Leu Trp Gln Phe Leu Leu Glu Leu Ser Asp Ser Ala Asn  
 305 310 315 320  
 Ala Ser Cys Ile Thr Trp Glu Gly Thr Asn Gly Glu Phe Lys Met Thr  
 325 330 335

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Asp Pro Asp Glu Val Ala Arg Arg Trp Gly Gln Arg Lys Ser Lys Pro  
340 345 350

Asn Met Asn Tyr Asp Lys Leu Ser Arg Ala Leu Arg Tyr Tyr Asp  
355 360 365

Lys Asn Ile Met Thr Lys Val His Gly Lys Arg Tyr Ala Tyr Lys Phe  
370 375 380

Asp Phe His Gly Ile Ala Gln Ala Leu Gln Pro His Pro Thr Glu Ser  
385 390 395 400

Ser Met Tyr Lys Tyr Pro Ser Asp Ile Ser Tyr Met Pro Ser Tyr His  
405 410 415

Ala His Gln Gln Lys Val Asn Phe Val Pro Pro His Pro Ser Ser Met  
420 425 430

Pro Val Thr Ser Ser Ser Phe Phe Gly Ala Ala Ser Gln Tyr Trp Thr  
435 440 445

Ser Pro Thr Gly Gly Ile Tyr Pro Asn Pro Asn Val Pro Arg His Pro  
450 455 460

Asn Thr His Val Pro Ser His Leu Gly Ser Tyr Tyr  
465 470 475

&lt;210&gt; 147

&lt;211&gt; 1431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 147

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atggcgctcca cggattacag tacctatagc caagctgcag cgcagcaggc ctacagtgtc 60
tacaccgccc agcccactca aggatatgca cagaccaccc aggcataatgg gcaacaagaac 120
tatggaaacct atggacagcc cactgatgtc agctataccc aggcctcagac cactgcaacc 180
tatgggcaga ccgcctatgc aactctttat ggacagcctc ccactgggtta tactactcca 240
actgcccccc aggcatacag ccagcctgtc cagggggtatg gcactgggtgc ttatgatacc 300
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cccagcctag gatattggaca gagtaactac agttatcccc aggtacctgg gagctacccc 540
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cccgcctac ctaaacccca cgtgcctcca cactaggga gctactacta g 1431

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&lt;210&gt; 148

&lt;211&gt; 154

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 148

Met Asp Leu Pro Tyr Tyr His Gly Arg Leu Thr Lys Gln Asp Cys Glu  
 1 5 10 15

Thr Leu Leu Leu Lys Glu Gly Val Asp Gly Asn Phe Leu Leu Arg Asp  
 20 25 30

Ser Glu Ser Ile Pro Gly Val Leu Cys Leu Cys Val Ser Phe Lys Asn  
 35 40 45

Ile Val Tyr Thr Tyr Arg Ile Phe Arg Glu Lys His Gly Tyr Tyr Arg  
 50 55 60

Ile Gln Pro Ile Lys Arg Thr Ser Pro Ser Leu Arg Trp Arg Gly Ser  
 65 70 75 80

Lys Leu Glu Leu Glu Ala Phe Met Thr Ala Glu Gly Ser Pro Lys Gln  
 85 90 95

Val Phe Pro Ser Leu Lys Glu Leu Ile Ser Lys Phe Glu Lys Pro Asn  
 100 105 110

Gln Gly Met Val Val His Leu Leu Lys Pro Ile Lys Arg Thr Ser Pro  
 115 120 125

Ser Leu Arg Trp Arg Gly Leu Lys Leu Glu Leu Glu Thr Phe Val Asn  
 130 135 140

Ser Asn Ser Asp Tyr Val Asp Val Leu Pro  
 145 150

&lt;210&gt; 149

&lt;211&gt; 465

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 149

atggatctgc cttactacca tggacgtctg accaagcaag actgtgagac cttgctgctc 60  
 aaggaagggg tggatggcaa ctttctttta agagacagcg agtcgatacc aggagtcctg 120  
 tgcctctctg tctcgtttta aatatattgc tacacatacc gaatctctcag agagaacac 180  
 gggattacca ggatacagcc aataaagaga accagcccca gcttgagatg gagaggatcg 240  
 aaattagagt tggagacatt tatgactgca gaaggttctc caaaacaggc ctttccaagc 300  
 ctaaaggaac tgatctccaa attgaaaaa ccaatcagg ggatgggtgt tcacctttta 360  
 aagccaataa agagaaccag cccagcttg agatggagag gattgaaatt agagttggaa 420  
 acatttgtga acagtaacag cgattattgtg gatgtcttgc cttga 465

&lt;210&gt; 150

&lt;211&gt; 132

&lt;212&gt; PRT

118/299

&lt;213&gt; Homo sapiens

&lt;400&gt; 150

```

Met Asp Leu Pro Tyr Tyr His Gly Arg Leu Thr Lys Gln Asp Cys Glu
 1             5             10             15

Thr Leu Leu Leu Lys Glu Gly Val Asp Gly Asn Phe Leu Leu Arg Asp
                20             25             30

Ser Glu Ser Ile Pro Gly Val Leu Cys Leu Cys Val Ser Phe Lys Asn
 35             40             45

Ile Val Tyr Thr Tyr Arg Ile Phe Arg Glu Lys His Gly Tyr Tyr Arg
 50             55             60

Ile Gln Thr Ala Glu Gly Ser Pro Lys Gln Val Phe Pro Ser Leu Lys
 65             70             75             80

Glu Leu Ile Ser Lys Phe Glu Lys Pro Asn Gln Gly Met Val Val His
 85             90             95

Leu Leu Lys Pro Ile Lys Arg Thr Ser Pro Ser Leu Arg Trp Arg Gly
100            105            110

Leu Lys Leu Glu Leu Glu Thr Phe Val Asn Ser Asn Ser Asp Tyr Val
115            120            125

Asp Val Leu Pro
130

```

&lt;210&gt; 151

&lt;211&gt; 420

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 151

```

atggatctgc cttactacca tggacgtctg accaagcaag actgtgagac cttgctgctc 60
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tgcctctctgt tctcgtttta aaatattgtc tacacatacc gaatctttcag agagaacac 180
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gtgaacagta acagcgatta tgtggatgtc ttgccttgaa gataaggctg ccggacaaa 420

```

&lt;210&gt; 152

&lt;211&gt; 45

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 152

```

Met Asp Leu Pro Tyr Tyr His Gly Arg Leu Thr Lys Gln Asp Cys Glu
 1             5             10             15

Thr Leu Leu Leu Lys Glu Gly Val Asp Gly Asn Phe Leu Leu Arg Asp
                20             25             30

```

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Ser Glu Ser Ile Pro Gly Val Leu Cys Leu Cys Val Ser  
 35 40 45

<210> 153  
 <211> 136  
 <212> DNA  
 <213> Homo sapiens

<400> 153  
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 aaggaagggg tggatggcaa ctttctttaa agagacagcg agtcgatacc aggagtcctg 120  
 tgccctctgtg tctcgt 136

<210> 154  
 <211> 132  
 <212> FRT  
 <213> Mus musculus

<400> 154  
 Met Asp Leu Pro Tyr Tyr His Gly Cys Leu Thr Lys Arg Glu Cys Glu  
 1 5 10 15

Ala Leu Leu Leu Lys Gly Gly Val Asp Gly Asn Phe Leu Ile Arg Asp  
 20 25 30

Ser Glu Ser Val Pro Gly Ala Leu Cys Leu Cys Val Ser Phe Lys Lys  
 35 40 45

Leu Val Tyr Ser Tyr Arg Ile Phe Arg Glu Lys His Gly Tyr Tyr Arg  
 50 55 60

Ile Glu Thr Asp Ala His Thr Pro Arg Thr Ile Phe Pro Asn Leu Gln  
 65 70 75 80

Glu Leu Val Ser Lys Tyr Gly Lys Pro Gly Gln Gly Leu Val Val His  
 85 90 95

Leu Ser Asn Pro Ile Met Arg Asn Asn Leu Cys Gln Arg Gly Arg Arg  
 100 105 110

Met Glu Leu Glu Leu Asn Val Tyr Glu Asn Thr Asp Glu Glu Tyr Val  
 115 120 125

Asp Val Leu Pro  
 130

<210> 155  
 <211> 399  
 <212> DNA  
 <213> Mus musculus

<400> 155  
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 tgcctctgtg tctcgtttaa aaagcttgctc tacagctacc gaatcttcag agagaaacat 180

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```

ggatattaca ggatagagac tgaatgctcat actccaagaa cgatctttcc aaacctacag 240
gaattggtct ccaaatatgg aaaaaccgggt caaggattgg tggttcacct ttcaaaccca 300
ataatgagaa acaacctatg ccaaagaggg agaagaatgg agttagagct gaatgtttat 360
gagaacactg atgaggagta tgtggagctc ttgccttga 399

```

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<210> 156
<211> 76
<212> PRT
<213> Homo sapiens

```

```

<400> 156
Pro Thr Ser Tyr Pro Pro Gln Thr Gly Ser Tyr Ser Gln Ala Pro Ser
  1             5             10             15

Gln Tyr Ser Gln Gln Ser Ser Ser Tyr Gly Gln Gln Asn Pro Tyr Gln
          20             25             30

Ile Leu Gly Pro Thr Ser Ser Arg Leu Ala Asn Pro Gly Ser Gly Gln
      35             40             45

Ile Gln Leu Trp Gln Phe Leu Leu Glu Leu Leu Ser Asp Ser Ala Asn
      50             55             60

Ala Ser Cys Ile Thr Trp Glu Gly Thr Asn Gly Glu
      65             70             75

```

```

<210> 157
<211> 229
<212> DNA
<213> Homo sapiens

```

```

<400> 157
cccactagtt acccacccca aactggatcc tacagccaag ctccaagtca atatagccaa 60
cagagcagca gctacgggca gcagaatccg tatcagatcc tgggcccagac cagcagtcgc 120
ctagccaacc ctggaagcgg gcagatccag ctgtggcaat tcctcctgga gctgctctcc 180
gacagcgcca acgccagctg tatcacctgg gaggggacca acgggggagt 229

```

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<210> 158
<211> 100
<212> DNA
<213> Homo sapiens

```

```

<400> 158
tacgggcagc agagttcact gctggcctat aatacaacct ccacaccga ccaatcctca 60
cgattgagtg tcaagaaga cccttcttat gactcagtc 100

```

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<210> 159
<211> 20
<212> PRT
<213> Homo sapiens

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```

<400> 159
Ser Gln Gln Ser Ser Tyr Gly Gln Gln Ser Pro Pro Leu Gly Gly
  1             5             10             15

```

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Ala Gln Thr Ile  
20

&lt;210&gt; 160

&lt;211&gt; 60

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 160

agccaacaga gcagcagcta cgggcagcag agtctctccc ttggaggggc acaaacgata 60

&lt;210&gt; 161

&lt;211&gt; 447

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 161

agatagagct ggagacctac aaactgaagt gcaaggcact gcaggaggag aaccgcgacc 60  
 tggcgaagc cagcgctacc atcatactgg agaacaggcc atctgttctg ttctacctg 120  
 tccccggag gctgcccaga aaccggccct cgtgggactc catggagaac caggtctccg 180  
 tggatgcctt caagatcctg gaggatccaa agtgggaatt cctcggaag aacttggttc 240  
 ttggaaaaaac tctaggagaa ggcgaatttg gaaaagtggc caaggcaacg gcttccatc 300  
 tgaaaggcag agcagggtag accacgggtg ccgtgaagat gctgaaagag aacgcctccc 360  
 cgagtgcgtc tcgagacctg ctgtcagagt tcaacgtctc gaagcaggtc aaccaccacc 420  
 atgtcatcaa attgtatggg gcctgca 447

&lt;210&gt; 162

&lt;211&gt; 585

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 162

Met Ala Asp Ser Ala Ser Glu Ser Asp Thr Asp Gly Ala Gly Gly Asn  
 1 5 10 15

Ser Ser Ser Ser Ala Ala Met Gln Ser Ser Cys Ser Ser Thr Ser Gly  
 20 25 30

Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Lys Ser Gly Gly  
 35 40 45

Ile Val Ile Ser Pro Phe Arg Leu Glu Glu Leu Thr Asn Arg Leu Ala  
 50 55 60

Ser Leu Gln Gln Glu Asn Lys Val Leu Lys Ile Glu Leu Glu Thr Tyr  
 65 70 75 80

Lys Leu Lys Cys Lys Ala Leu Gln Glu Glu Asn Arg Asp Leu Arg Lys  
 85 90 95

Ala Ser Val Thr Ile Gln Ala Arg Ala Glu Gln Glu Glu Glu Phe Ile  
 100 105 110

Ser Asn Thr Leu Phe Lys Lys Ile Gln Ala Leu Gln Lys Glu Lys Glu



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115	120	125
Thr Leu Ala Val Asn Tyr Glu Lys Glu Glu Glu Phe Leu Thr Asn Glu		
130	135	140
Leu Ser Arg Lys Leu Met Gln Leu Gln His Glu Lys Gly Glu Leu Glu		
145	150	155
Gln His Leu Glu Gln Glu Gln Glu Phe Gln Val Asn Lys Leu Met Lys		
165	170	175
Lys Ile Lys Lys Leu Glu Asn Asp Thr Ile Ser Lys Gln Leu Thr Leu		
180	185	190
Glu Gln Leu Arg Arg Glu Lys Ile Asp Leu Glu Asn Thr Leu Glu Gln		
195	200	205
Glu Gln Glu Ala Leu Val Asn Arg Leu Trp Lys Arg Met Asp Lys Leu		
210	215	220
Glu Ala Glu Thr Arg Ile Leu Gln Glu Lys Leu Asp Gln Pro Val Ser		
225	230	235
Ala Pro Pro Ser Pro Arg Asp Ile Ser Met Glu Ile Asp Ser Pro Glu		
245	250	255
Asn Met Met Arg His Ile Arg Phe Leu Lys Asn Glu Val Glu Arg Leu		
260	265	270
Lys Lys Gln Leu Arg Ala Ala Gln Leu Gln His Ser Glu Lys Met Ala		
275	280	285
Gln Tyr Leu Glu Glu Glu Arg His Met Arg Glu Glu Asn Leu Arg Leu		
290	295	300
Gln Arg Lys Leu Gln Arg Glu Met Glu Arg Arg Glu Ala Leu Cys Arg		
305	310	315
Gln Leu Ser Glu Ser Glu Ser Ser Leu Glu Met Asp Asp Glu Arg Tyr		
325	330	335
Phe Asn Glu Met Ser Ala Gln Gly Leu Arg Pro Arg Thr Val Ser Ser		
340	345	350
Pro Ile Pro Tyr Thr Pro Ser Pro Ser Ser Ser Arg Pro Ile Ser Pro		
355	360	365
Gly Leu Ser Tyr Ala Ser His Thr Val Gly Phe Thr Pro Pro Thr Ser		
370	375	380
Leu Thr Arg Ala Gly Met Ser Tyr Tyr Asn Ser Pro Gly Leu His Val		
385	390	395
Gln His Met Gly Thr Ser His Gly Ile Thr Arg Pro Ser Pro Arg Arg		
405	410	415
Ser Asn Ser Pro Asp Lys Phe Lys Arg Pro Thr Pro Pro Pro Ser Pro		
420	425	430

Asn Thr Gln Thr Pro Val Gln Pro Pro Pro Pro Pro Pro Pro Pro  
435 440 445

Met Gln Pro Thr Val Pro Ser Gly Ser His Leu Ala Ala Tyr Ser Phe  
450 455 460

Ala Thr Phe Gly Ala His Leu Leu Pro Ala Leu Met His Glu Leu Ser  
465 470 475 480

Leu Asn Phe Lys Leu Gly Leu Ile Gln Trp Ser Arg Leu Leu Asn Ala  
485 490 495

Lys Gly Ser Phe Ser Gly Ile Phe Gly Tyr Asp Leu Phe Ala Leu Arg  
500 505 510

Leu Ser Arg Leu His Tyr Pro Leu Cys Cys Lys Cys Leu Ser Glu Met  
515 520 525

Gln Pro Val Leu Trp Val Tyr Asn Thr Asn Gln Thr Thr Phe Ser Ile  
530 535 540

Ser Val Leu Leu Glu Ser Ser Cys Thr Ser Ile Pro Trp Leu Glu Pro  
545 550 555 560

Ser Leu Phe Gly Ile Trp Tyr Phe Ser Ser Ser Val Gln Phe Leu Leu  
565 570 575

Gly Pro Glu Leu His Ser Pro Gly Phe  
580 585

<210> 163

<211> 3011

<212> DNA

<213> Homo sapiens

<400> 163

ctgctgctcc tctctctttc ccagcccgcc gcggccatgg cggacagcgc cagcgagagc 60  
gacacggacg gggcgggggg caacagcagc agctcgccgc ccatgcagtc gtctctgctc 120  
tcgacctcgg gcggcgccgg tggcgccggg ggagcgccgc gcggtgggaa gtccgggggc 180  
attgtcatct cgcggttcgc cctggaggag ctccaccaacc gctcgccctc gctgcagcaa 240  
gagaacaagg tgctgaagat agagctggag acctacaaac tgaagtgcga ggcactgcag 300  
gaggagaacc ggcacctgcg caaagccagc gttaccatcc aagccagggc tgagcaggaa 360  
gaagaattca ttagttaaac ttatttcaag aaaatttcagg ctttgcagaa ggagaaagaa 420  
accttctgct taaattatga gaaagaagaa gaattctcca ctaatgagct ctccagaaaa 480  
ttgatcagtg tgcagcatga gaaaggcgaa ctagaacagc atcttgaaca agagcaggaa 540  
tttcagggtca acaaaactgat gaagaaaatt aaaaaactgg agaatacac catttctaag 600  
caacttacct tagaacagtt gagacgggag aagattgacc ttgaaaatac attggaacaa 660  
gaacaagaag cactagttaa tcgcctctgg aaaaggatgg ataagcttga agctgaaacg 720  
cgaatcctgc aggaaaaaatt agaccagccc gtctctgctc caccatcgcc tagagatatc 780  
tccatggaga ttgattctcc agaaaaatg atgcgtcaca tcaggttttt aaagaatgaa 840  
gtggaacggc tgaagaagca actgagagct gctcagttac agcattcaga gaaaatggca 900  
cagttatctgg agggaggaa ctcacatgaga gaagagaact tgaggctcca gaggaagctg 960  
cagaggagga tggagagacg agaagccctc tgcgcagacc tctccgagag taggtccagc 1020  
ttagaaatgg acgacgaaag gtatttttaat gagatgtctg cacaaggatt aagacctcga 1080  
actgtgtcca gcccgatccc ttacacacct tctccgagtt caagcaggcc tatatcacct 1140  
ggctatcatc atgcaagta cgcggttggt ttccagccac caacttcaat gactagagct 1200

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```

ggaatgtctt attacaattc ccgggtctt cactgcagc acatgggaac atcccatggt 1260
atcacaggc cttaccacg gagaagcaac agtcctgaca aattcaaacg gccacgcgcg 1320
ctcccatctc ccaacacaca gaccccgctc cagccacctc cactccacc tccgccacc 1380
atgcagccca cgggtccctc aggcagccac ctgcagcctc actccttcgc aacattcggc 1440
gcacacctcc tccagcctt aatgcatgag cttagctga atttcaagtt gggactcctc 1500
caatggagcc gtctactcaa cgccaaaggt tcttctctg gcataatttg atatgactta 1560
tttgcactga ggttatctag gcttcaactat ccattgtgtt gtaaatgttt gtcagaaatg 1620
cagccagctg tgtgggtcta caacactaac cagacgactt tttccatcag tgttttactt 1680
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aaaaaataaa gggatatctt ttttatattt ttttccatga atcgcagaaa aataactaag 1860
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acaattcaga cttttgaaaa tctggcttcc agtgtagaac agaaagttag atgaatcagt 1980
gcccaagaca tatttctctg ttaacagaaac tttctacaga tacatttttt acaggttatt 2040
ttcatttgtt tattgacatc catgtctctc gtaaacagag gtcccaaagt aatgaatcat 2100
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tgtctacttc acoggtgggt tcaatggcta attagaatgt gttatttgat tctcgtgcga 2280
gaaggcagtg tgattgttaac aaaaacaagt cggcttcccc ctctcgtact tcatattgtg 2340
ttctctaaaa tagagtttga acaaatattt taaagggtga aataccatt agaaaaatct 2400
atttgaatag gacattatcg cattatcttg gcataatggc cagaaaaatat tgtattgctt 2460
ggcagaaagta aaaaataagt ctaaaggaaa gtacacatt agcattgatg gctgttcatt 2520
tcacccagta taagcaagtg tacaaagaag tatattctga atacattatt tccattcatt 2580
tagcacaat aaatcatttg gtttcaactt gcagtggaac actgagtcac tcttttctta 2640
atacgtgcaa catcttaatt ttgtttttc agcagttgct gttttgact ttggtagtga 2700
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agagaatga tattttatga caagaatgtg tatctgttgg gatataatca gagaactgaa 2820
aagtaattta tcagtaattt ttaagatgoc atgttttttg acaaccatct ctaatatgca 2880
actctttatt aaacacactc ctaaaaataa ggaaccatga cgattgtaga ttttaatat 2940
tgtacagtat agaaacctcc gatttttgc ttcgaatgca gtatttaaga gtaaacagaa 3000
aaaaaaaaa a 3011

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<210> 164  
 <211> 447  
 <212> DNA  
 <213> Homo sapiens

```

<400> 164
gatcaggggg ctggagggcc ctcccttgga acacgtgtgg ctggcgagct ggtgggtcgg 60
gggcagtcct tgggtttccc gcacccgcag tgcctgcgcg ttcccagccc gcccggtgct 120
accagacggc ggccggcggg tcccgagctc ttccagccagc tttgctgggc ggccttaggga 180
gcgcgccacg ccggctcgga gcgagcccca gtgcaatact gcccagcccc gggcggggtc 240
tctgtctctc ggcagaggag gtcccttggc agcgggaggg gccctctctt tctctcggcg 300
ccgctcgag tctcgccctt ggtgccaggg gctcagctcg gcgctccctt gctgctcgcc 360
ggcgccact cattcgagc cgggccttgc tgcgcgcgc ctccctcgtg ctctctctcc 420
tttcccagc ccgcgcggcg catggcg 447

```

<210> 165  
 <211> 585  
 <212> PRT  
 <213> Homo sapiens

```

<400> 165
Met Ala Asp Ser Ala Ser Glu Ser Asp Thr Asp Gly Ala Gly Gly Asn
1 5 10 15

```

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Ser Ser Ser Ser Ala Ala Met Gln Ser Ser Cys Ser Ser Thr Ser Gly  
 20 25 30  
 Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Lys Ser Gly Gly  
 35 40 45  
 Ile Val Ile Ser Pro Phe Arg Leu Glu Glu Leu Thr Asn Arg Leu Ala  
 50 55 60  
 Ser Leu Gln Gln Glu Asn Lys Val Leu Lys Ile Glu Leu Glu Thr Tyr  
 65 70 75 80  
 Lys Leu Lys Cys Lys Ala Leu Gln Glu Glu Asn Arg Asp Leu Arg Lys  
 85 90 95  
 Ala Ser Val Thr Ile Gln Ala Arg Ala Glu Gln Glu Glu Glu Phe Ile  
 100 105 110  
 Ser Asn Thr Leu Phe Lys Lys Ile Gln Ala Leu Gln Lys Glu Lys Glu  
 115 120 125  
 Thr Leu Ala Val Asn Tyr Glu Lys Glu Glu Glu Phe Leu Thr Asn Glu  
 130 135 140  
 Leu Ser Arg Lys Leu Met Gln Leu Gln His Glu Lys Gly Glu Leu Glu  
 145 150 155 160  
 Gln His Leu Glu Gln Glu Gln Glu Phe Gln Val Asn Lys Leu Met Lys  
 165 170 175  
 Lys Ile Lys Lys Leu Glu Asn Asp Thr Ile Ser Lys Gln Leu Thr Leu  
 180 185 190  
 Glu Gln Leu Arg Arg Glu Lys Ile Asp Leu Glu Asn Thr Leu Glu Gln  
 195 200 205  
 Glu Gln Glu Ala Leu Val Asn Arg Leu Trp Lys Arg Met Asp Lys Leu  
 210 215 220  
 Glu Ala Glu Thr Arg Ile Leu Gln Glu Lys Leu Asp Gln Pro Val Ser  
 225 230 235 240  
 Ala Pro Pro Ser Pro Arg Asp Ile Ser Met Glu Ile Asp Ser Pro Glu  
 245 250 255  
 Asn Met Met Arg His Ile Arg Phe Leu Lys Asn Glu Val Glu Arg Leu  
 260 265 270  
 Lys Lys Gln Leu Arg Ala Ala Gln Leu Gln His Ser Glu Lys Met Ala  
 275 280 285  
 Gln Tyr Leu Glu Glu Glu Arg His Met Arg Glu Glu Asn Leu Arg Leu  
 290 295 300  
 Gln Arg Lys Leu Gln Arg Glu Met Glu Arg Arg Glu Ala Leu Cys Arg  
 305 310 315 320  
 Gln Leu Ser Glu Ser Glu Ser Ser Leu Glu Met Asp Asp Glu Arg Tyr

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325                      330                      335  
 Phe Asn Glu Met Ser Ala Gln Gly Leu Arg Pro Arg Thr Val Ser Ser  
                          340                      345                      350  
 Pro Ile Pro Tyr Thr Pro Ser Pro Ser Ser Arg Pro Ile Ser Pro  
                          355                      360                      365  
 Gly Leu Ser Tyr Ala Ser His Thr Val Gly Phe Thr Pro Pro Thr Ser  
                          370                      375                      380  
 Leu Thr Arg Ala Gly Met Ser Tyr Tyr Asn Ser Pro Gly Leu His Val  
                          385                      390                      395                      400  
 Gln His Met Gly Thr Ser His Gly Ile Thr Arg Pro Ser Pro Arg Arg  
                          405                      410                      415  
 Ser Asn Ser Pro Asp Lys Phe Lys Arg Pro Thr Pro Pro Pro Ser Pro  
                          420                      425                      430  
 Asn Thr Gln Thr Pro Val Gln Pro Pro Pro Pro Pro Pro Pro Pro  
                          435                      440                      445  
 Met Gln Pro Thr Val Pro Ser Gly Ser His Leu Ala Ala Tyr Ser Phe  
                          450                      455                      460  
 Ala Thr Phe Gly Ala His Leu Leu Pro Ala Leu Met His Glu Leu Ser  
                          465                      470                      475                      480  
 Leu Asn Phe Lys Leu Gly Leu Ile Gln Trp Ser Arg Leu Leu Asn Ala  
                          485                      490                      495  
 Lys Gly Ser Phe Ser Gly Ile Phe Gly Tyr Asp Leu Phe Ala Leu Arg  
                          500                      505                      510  
 Leu Ser Arg Leu His Tyr Pro Leu Cys Cys Lys Cys Leu Ser Glu Met  
                          515                      520                      525  
 Gln Pro Val Leu Trp Val Tyr Asn Thr Asn Gln Thr Thr Phe Ser Ile  
                          530                      535                      540  
 Ser Val Leu Leu Glu Ser Ser Cys Thr Ser Ile Pro Trp Leu Glu Pro  
                          545                      550                      555                      560  
 Ser Leu Phe Gly Ile Trp Tyr Phe Ser Ser Ser Val Gln Phe Leu Leu  
                          565                      570                      575  
 Gly Pro Glu Leu His Ser Pro Gly Phe  
                          580                      585

&lt;210&gt; 166

&lt;211&gt; 3011

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 166

ctgctgctcc tcctcctttc ccagcccgcc gcggccatgg cggacagcgc cagcgagagc 60

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gacacggcagc gggcgggggg caacagcagc agtcggggcg ccatgcagtc gtcctgctgc 120
tcgacctcgg gggcgggggg tggcgggggg gggcgggggg ggggtgggaa gtcggggggg 180
atgttcacat cgcgcttcog cctggaggag ctccaccaac gctcgacctc gtcgagcaa 240
gagaacaagg tgcctgaagt agagctggag acctacaaac tgaagtgcac ggcactcgag 300
gaggagaacc gogagctcgc caaagccagc gttaccatcc aagccaggag tggcgaggaa 360
gaagaaattca ttagtacaac ttattccaag aaattccagg ctttgcagaa gggagaaaga 420
acccttgctg taaattatga gaagaagaa gaattcctca taatgagct ctccagaaaa 480
tgtagtcagt tcgacagtga gaagggcgaa ctagaacagc atcttgaaca agagcaggaa 540
ttccagctca aaaaactgat gaagaaaaat aaaaactgg agaattgacac catttctaag 600
caactacatc tagaacaagt gtagcgggag aagattgacc ttgaaaaatac atttgaaaca 660
gaacaagaag caactagttaa togcctctgg aaaaaggatg ataagcttga agctgaaacg 720
cgaactctgc aggaaaaaat agaccagccc gtcctctgct caccatcgcc tagagatac 780
tccatggaga ttgattctcc agaaaaatat atgcgtcaca tcagggtttt aagaagatac 840
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cagatctcgg agggaggaa g tccatgaga gaagagaact tgaggctcca gaggaagctg 960
cagagggaga tggagagacg agaagccctc tctccgagag tctccgagag gaggctccag 1020
ttagaaatgg acgacgaaag gtattttaat gagatgtctg cacaaggatt aagaactaga 1080
actgtgtcca gcccgatccc ttacacacct tctccgagtt caagcaggcc tatctcact 1140
ggtctatcat atgcaagtca cccggttggt ttcaogccac caacttcaat gactagagct 1200
ggaatgtctt attacaattc cccgggtctt cactggcagc actggggaac atccctaggt 1260
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cctccatctc ccaacacaca gaccccgctc cagccacctc caccctccac tccgcacccc 1380
atgcagccca oggtccccctc aggcagccac ctgcagcctc actccttcgc aacattcggc 1440
gcacacaccc tcccagcctt aatgcattgag cttagcttga atttcaagtt gggactccat 1500
caatggagcc gtctactcaa cgcocaaagg tctctctctg gcatatttgg atatgactta 1560
tttgactcga ggttatctag gcttcactat ccaattgtgt gtaaatgttt gtcagaaagt 1620
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gaatcttcat gtaactccat tccctggctg gaaccttcgc tggttggtaa ttggatttcc 1740
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ctgttgtaac cctcctataa ttataatagt gtttacaacac aataccaata atctcagcact 1920
acaattcaga cctttgaaaa tctggcttcc agtgtagaac agaaagttag atgaactcag 1980
gcccaagaca tatttctcgt ttaacgaac tttctacaga taactttttt acagggttatt 2040
ttcatttgtt tattgacatc catgtctctc gtaaacagag gtcccagaag aatgaatcac 2100
gtggcgtaac ttctccacat aaatggatgg ataattacgt atattaagat gtgattctct 2160
tttttatcct taatgttaat ctacttaacc tggcccccct taacatgagt taacatagat 2220
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gaaggcagtg tgattgtaac aaaaacaatg oggcttcccc ttctgttaac ttatttgtgt 2340
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tcaccacgta taagcaagtg tacaagaag tatattctga atacattatt tccattcatt 2580
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atacgtgcac catcttaatt tttgttttcc agcagttgct gttttgtaa ttggtagtga 2700
agtgattttt acocactgtg ttgtcatatt tatatatgt tctggtatga ataatctact 2760
agagaattga tattttatga caagaatgtg tatctgttgg gatataatca gagaactcgaa 2820
aagtaattta tcaagtaatt ttaagagctc atgttttggc ataacactct ctaatagcca 2880
actctttatt aaacacactc ctaaaaataa ggaacctatga cgaattgtaga tattttaat 2940
tgtacagtat agaaaactcc gatttttgce ttogaatgca gttatttaaga gtttaacaga 3000
aaaaaaaaa a 3011

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&lt;210&gt; 167

&lt;211&gt; 808

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 167

128/299

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agatcttcac  tgaccatggt  tgattttgca  gcatttggga  ttttgacagc  tgtagccatg  60
gcagtgtcga  cactgacctt  gactgtgggt  tcccaggga  tgtggggcca  gaccaggaca  120
gcccaggagc  aggagacctg  ggggtgacga  tgcccagagc  tggcacatca  agggagggtt  180
cctggatcat  ggcaggcttt  ggctccctgg  tcagagttca  agtactgggg  gccagggtgg  240
gggtctcgga  aggcaccccg  agcagtccca  agtggggccc  aatgtgtgga  tagaactttg  300
gtggaggcca  ggggtggtagt  gccagcagca  ggggtgagcg  gtgcgtgagg  gccagtgca  360
cccttgagga  gcagtgtatc  cacactctga  ggcggaacat  ggtggcgcc  ttctttgcag  420
gggtggctat  gtgagaaagt  tgtcctggac  acttccactg  tagtcggagg  tcctggcgct  480
ggcctgtgtc  tcattttagt  ctggggcagg  ggtcagggga  gacagttagc  caggaaccag  540
agagggttga  agtaactgagt  ccaagccatg  ctgtgaccac  acctgtcatg  tagcagcttt  600
caggggctcg  gctgtggsgt  cccgcccagg  gcagagacag  gcagggtcgg  ctggctcaga  660
tgacagccgg  ttctctgcac  attggaactt  gtccatgggg  cctcctttaa  ggtctttgcc  720
ttcttctcnc  cctgtcatcc  tcacaacttt  ccccctctt  ctecccttc  cctcatttcc  780
aacataggag  gatccaaagt  ggggaattc

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&lt;210&gt; 168

&lt;211&gt; 271

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 168

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Met Glu Asp Ser His Lys Ser Thr Thr Ser Glu Thr Ala Pro Gln Pro
  1              5              10              15

Gly Ser Ala Val Gln Gly Ala His Ile Ser His Ile Ala Gln Gln Val
  20              25              30

Ser Ser Leu Ser Glu Ser Glu Glu Ser Gln Asp Ser Ser Asp Ser Ile
  35              40              45

Gly Ser Ser Gln Lys Ala His Gly Ile Leu Ala Arg Arg Pro Ser Tyr
  50              55              60

Arg Lys Ile Leu Lys Asp Leu Ser Ser Glu Asp Thr Arg Gly Arg Lys
  65              70              75              80

Gly Asp Gly Glu Asn Ser Gly Val Ser Ala Ala Val Thr Ser Met Ser
  85              90              95

Val Pro Thr Pro Ile Tyr Gln Thr Ser Ser Gly Gln Tyr Ile Ala Ile
  100             105             110

Ala Pro Asn Gly Ala Leu Gln Leu Ala Ser Pro Gly Thr Asp Gly Val
  115             120             125

Gln Gly Leu Gln Thr Leu Thr Met Thr Asn Ser Gly Ser Thr Gln Gln
  130             135             140

Gly Thr Thr Ile Leu Gln Tyr Ala Gln Thr Ser Asp Gly Gln Gln Ile
  145             150             155             160

Leu Val Pro Ser Asn Gln Val Val Val Gln Thr Ala Ser Gly Asp Met
  165             170             175

Gln Thr Tyr Gln Ile Arg Thr Thr Pro Ser Ala Thr Ser Leu Pro Gln
  180             185             190

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Thr Val Val Met Thr Ser Pro Val Thr Leu Thr Ser Gln Thr Thr Lys  
195 200 205

Thr Asp Asp Pro Gln Leu Lys Arg Glu Ile Arg Leu Met Lys Asn Arg  
210 215 220

Glu Ala Ala Arg Glu Cys Arg Arg Lys Lys Lys Glu Tyr Val Lys Cys  
225 230 235 240

Leu Glu Asn Arg Val Ala Val Leu Glu Asn Gln Asn Lys Thr Leu Ile  
245 250 255

Glu Glu Leu Lys Thr Leu Lys Asp Leu Tyr Ser Asn Lys Ser Val  
260 265 270

&lt;210&gt; 169

&lt;211&gt; 816

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 169

atggaagatt cccacaagag taccacgtca gagacagcac ctcaacctgg ttcagcagtt 60  
cagggagctc acattttctca tattgtctcaa caggtatcat ctttatcaga aagtggaggag 120  
tcccaggact catccgacag cataggctcc tcacagaaag cccacgggat cctagcacgg 180  
gcgccatctt acagaaaaat ttgaaagac ttatctcttg aagatcacag gggcagaaaa 240  
ggagacggag aaaattcttg agttctctgt gctgtcactt ctatgtctgt tccaactccc 300  
cttatctcaga ctacagcagg acagtacatt gccattgccc caaatggagc cttacagttg 360  
gcaagtcacg gcacagatgg agtacaggga cttcagacat taaccatgac aaattcaggc 420  
agtaactcagc aaggtacaac tattcttcag tatgcacaga cctctgatgg acagcagata 480  
cttgtgccca gcaatcaggt ggtcgtacaa actgcacag gagatgatgca aacataatcg 540  
atccgaacta cactctcagc taactctctg ccacaaactg tggatgatgac atctctctgt 600  
actctcacct ctcagacaac taagacagat gacccccaat tgaaaagaga aataagggtta 660  
atgaaaaaca gagaagctgc tcgagaaatg cgcagaaaga agaaaagaata tgtgaaatgc 720  
ctggaaaacc gagttgcagt cctggaatat caaataaaaa ctctaataga agagttaaaa 780  
actttgaagg atcttttatt caataaaagt gtttga 816

&lt;210&gt; 170

&lt;211&gt; 117

&lt;212&gt; FRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 170

Thr Gly Ser Tyr Ser Gln Ala Pro Ser Gln Tyr Ser Gln Gln Ser Ser  
1 5 10 15

Ser Tyr Gly Gln Gln Ile Ala Ile Ala Pro Asn Gly Ala Leu Gln Leu  
20 25 30

Ala Ser Pro Gly Thr Asp Gly Val Gln Gly Leu Gln Thr Leu Thr Met  
35 40 45

Thr Asn Ser Gly Ser Thr Gln Gln Gly Thr Thr Ile Leu Gln Tyr Ala  
50 55 60

Gln Thr Ser Asp Gly Gln Gln Ile Leu Val Pro Ser Asn Gln Val Val  
65 70 75 80



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Val Gln Thr Ala Ser Gly Asp Met Pro Thr Tyr Gln Ile Arg Thr Thr  
85 95

Pro Ser Ala Thr Ser Leu Pro Gln Thr Val Val Met Thr Ser Pro Val  
100 105 110

Thr Leu Thr Ser Gln  
115

&lt;210&gt; 171

&lt;211&gt; 353

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 171

aactggatcc tacagccaag ctccaagtca atatagccaa cagagcagca gctacgggca 60  
gcagattgcc attgcccac atggagcctt acagttggca agtccaggca cagatggagt 120  
acagggactt cagacattaa ccattgacaaa ttccaggcagt actcagcaag gtacaactat 180  
tcttcagtat gcacagacct ctgatggaca gcagatactt gtgccagca atcaggtggt 240  
cgtaacaact gcacaggag atatgccaac atatcagatc cgaactacac ctccagctac 300  
ttctctgccca caaactgtgg tgatgacatc tctctgtgact ctccactctc aga 353

&lt;210&gt; 172

&lt;211&gt; 500

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 172

taagtgccac ggagaaagct aaagcagaga aaggaatgga gaatgttcag gatggaggtc 60  
agagtgttac atcaggtggt caggaattac cttaggtaat tctccactc caaaccttc 120  
agtgacttcc atgacatgaa ataggaagtc attggagggt ttgagcagag gaatgacctg 180  
ttttaaaagg ctccactcagg ctgctgtatg gtgaatagag ttgcgaacag aggccatagg 240  
ataacagggt ttgttgaga aagtgttttc attttgaggg ctagggtgaa agacctgagg 300  
ttgtaccag tagtggagag ggaaggaaaa ttaactcagg gggagtgaat ctgtagaccc 360  
acttgagata agatactcgc tgggttaggt agggaggggca gataggatat ctaggcttgg 420  
agaggctggt aactcaaata taatggatgc ttaatTTTTT tttttttttt tgcagggggtg 480  
agcacagaca ggaatgcgag

&lt;210&gt; 173

&lt;211&gt; 521

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 173

ccctctaaac agatggccca ggagggggac caggtggctc tcacatgggt aagaaaggca 60  
gacctggtgc tagggagctg ggaccacaga atccttaatt ttccagcggg gaggctcggg 120  
gaacataggg gaattgggaa atgatagatc ttgtttcttt tgcctaggg ggtaactacg 180  
gggatgatcg tctgtgtggc agaggaggct atgatcgagg cggctaccgg ggccgcggcg 240  
gggacgtg aggtctccga gggggccggg gtgggtggga cagaggtggc ttggccctgt 300  
gcaagatgga ttccagacct tctgcagtc gaaagtctct gcagtaattt agagatggtg 360  
gtgaattgat ctgatttggg aacaatggaa ttagaagtgt ttgattctct ctaagcaagg 420  
gttttaaaaa ctacttttta aagaatgagt taaggggcgg gcattggtgc tcacacctgt 480  
aatcccagca ctttgggaga ccagaggtgt gtggatcacc t

521

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&lt;210&gt; 174

&lt;211&gt; 75

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 174

Tyr Ser Gln Gln Ser Ser Gln Pro Tyr Gly Gln Gln Ser Tyr Ser Gly  
 1 5 10 15

Tyr Ser Gln Ser Thr Asp Thr Ser Gly Tyr Gly Gln Ser Ser Tyr Ser  
 20 25 30

Ser Tyr Gly Gln Ser Gln Asn Met Phe Lys Lys Glu Val Tyr Leu His  
 35 40 45

Thr Ser Pro His Leu Lys Ala Asp Val Leu Phe Gln Thr Asp Pro Thr  
 50 55 60

Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser  
 65 70 75

&lt;210&gt; 175

&lt;211&gt; 225

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 175

tattcccagc agagcagtc gccctacgga cagcagagtt acagtgggta tagccagttc 60  
 acggacactt caggctatgg ccagagcagc tattttctt atggccagag ccagaacatg 120  
 ttcaagaagg aagtgtatct tcatacatca ccacacctga aagcagatgt gcttttccag 180  
 actgatccaa ctgcagagat ggcagctgag tcattgcctt tctccc 225

&lt;210&gt; 176

&lt;211&gt; 78

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 176

Gly Asp Trp Lys Cys Pro Asn Pro Thr Cys Glu Asn Met Asn Phe Ser  
 1 5 10 15

Trp Arg Asn Glu Cys Asn Gln Cys Lys Ala Pro Lys Pro Asp Gly Pro  
 20 25 30

Gly Gly Gly Pro Gly Gly Ser His Met Gly Val Phe Lys Lys Glu Val  
 35 40 45

Tyr Leu His Thr Ser Pro His Leu Lys Ala Asp Val Leu Phe Gln Thr  
 50 55 60

Asp Pro Thr Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser  
 65 70 75

&lt;210&gt; 177

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&lt;211&gt; 235

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 177

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tggtgactgg aagtgtccta atcccacctg tgagaatatg aacttctctt ggaggaatga 60
atgcaaccag tgtaaggccc ctaaaccaga tggcccaggga gggggaccag gtggctctca 120
catgggggtg ttcaagaagg aagtgtatct tcatacatca ccacacctga aagcagatgt 180
gctttttccag actgatccaa ctgcagagat ggcagctgag tcattgcctt tctcc 235

```

&lt;210&gt; 178

&lt;211&gt; 526

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 178

```

Met Ala Ser Asn Asp Tyr Thr Gln Gln Ala Thr Gln Ser Tyr Gly Ala
  1             5             10             15

```

```

Tyr Pro Thr Gln Pro Gly Gln Gly Tyr Ser Gln Gln Ser Ser Gln Pro
  20             25             30

```

```

Tyr Gly Gln Gln Ser Tyr Ser Gly Tyr Ser Gln Ser Thr Asp Thr Ser
  35             40             45

```

```

Gly Tyr Gly Gln Ser Ser Tyr Ser Ser Tyr Gly Gln Ser Gln Asn Thr
  50             55             60

```

```

Gly Tyr Gly Thr Gln Ser Thr Pro Gln Gly Tyr Gly Ser Thr Gly Gly
  65             70             75             80

```

```

Tyr Gly Ser Ser Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser
  85             90             95

```

```

Tyr Pro Gly Tyr Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser
  100            105            110

```

```

Tyr Gly Ser Ser Ser Gln Ser Ser Tyr Gly Gln Pro Gln Ser Gly
  115            120            125

```

```

Ser Tyr Ser Gln Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly
  130            135            140

```

```

Gln Gln Gln Ser Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln
  145            150            155            160

```

```

Tyr Asn Ser Ser Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn
  165            170            175

```

```

Tyr Gly Gln Asp Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly
  180            185            190

```

```

Gly Tyr Gly Asn Gln Asp Gln Ser Gly Gly Gly Gly Ser Gly Gly Tyr
  195            200            205

```

```

Gly Gln Gln Asp Arg Gly Gly Arg Gly Arg Gly Ser Gly Gly Gly
  210            215            220

```

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Gly Gly Gly Gly Gly Gly Tyr Asn Arg Ser Ser Gly Gly Tyr Glu  
 225 230 235 240  
 Pro Arg Gly Arg Gly Gly Gly Arg Gly Gly Arg Gly Gly Met Gly Gly  
 245 250 255  
 Ser Asp Arg Gly Gly Phe Asn Lys Phe Gly Gly Pro Arg Asp Gln Gly  
 260 265 270  
 Ser Arg His Asp Ser Glu Gln Asp Asn Ser Asp Asn Asn Thr Ile Phe  
 275 280 285  
 Val Gln Gly Leu Gly Glu Asn Val Thr Ile Glu Ser Val Ala Asp Tyr  
 290 295 300  
 Phe Lys Gln Ile Gly Ile Ile Lys Thr Asn Lys Lys Thr Gly Gln Pro  
 305 310 315 320  
 Met Ile Asn Leu Tyr Thr Asp Arg Glu Thr Gly Lys Leu Lys Gly Glu  
 325 330 335  
 Ala Thr Val Ser Phe Asp Asp Pro Pro Ser Ala Lys Ala Ala Ile Asp  
 340 345 350  
 Trp Phe Asp Gly Lys Glu Phe Ser Gly Asn Pro Ile Lys Val Ser Phe  
 355 360 365  
 Ala Thr Arg Arg Ala Asp Phe Asn Arg Gly Gly Gly Asn Gly Arg Gly  
 370 375 380  
 Gly Arg Gly Arg Gly Gly Pro Met Gly Arg Gly Gly Tyr Gly Gly Gly  
 385 390 395 400  
 Gly Ser Gly Gly Gly Gly Arg Gly Gly Phe Pro Ser Gly Gly Gly Gly  
 405 410 415  
 Gly Gly Gly Gln Gln Arg Ala Gly Asp Trp Lys Cys Pro Asn Pro Thr  
 420 425 430  
 Cys Glu Asn Met Asn Phe Ser Trp Arg Asn Glu Cys Asn Gln Cys Lys  
 435 440 445  
 Ala Pro Lys Pro Asp Gly Pro Gly Gly Gly Pro Gly Ser His Met  
 450 455 460  
 Gly Gly Asn Tyr Gly Asp Asp Arg Arg Gly Gly Arg Gly Gly Tyr Asp  
 465 470 475 480  
 Arg Gly Gly Tyr Arg Gly Arg Gly Gly Asp Arg Gly Gly Phe Arg Gly  
 485 490 495  
 Gly Arg Gly Gly Gly Asp Arg Gly Gly Phe Gly Pro Gly Lys Met Asp  
 500 505 510  
 Ser Arg Gly Glu His Arg Gln Asp Arg Arg Glu Arg Pro Tyr  
 515 520 525

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<210> 179  
 <211> 1824  
 <212> DNA  
 <213> Homo sapiens

<400> 179  
 atgctcagtc ctccaggcgt cgggtgctcag cgggtgttga acttcggttc ttgcttgcc 60  
 gtgcgcgcgt ggcgggacat ggcctcaaac gattataccc aacaagcaac ccaaaactat 120  
 ggggctacc ccaccagacc cgggcagggc tattcccagc agagcagtc ggcctaccga 180  
 cagcagagtt acagtggta tagccagtc ccggacactt caggctatgc ccagagcagc 240  
 tattctcttt atggccagag ccagaacaca ggctatggaa ctacgtcaac tcccaggaga 300  
 tatggctcga ctggcgggcta tggcagtagc cagagctccc aatcgctcta cgggcagcag 360  
 tccctccatcc ctggctatgg ccagcagcca gctcccagca gcacctcggg aagttacggg 420  
 agcagttctc agagcagcag ctatgggcag ccccagagtg ggagctacag ccagcagcct 480  
 agctatgggt gacagcagca aagctatgga cagcagcaaa gctataatcc ccctcagggc 540  
 tatggcagc agaacagcta caacagcagc agtgggtggg gaggtggagg tggagggtgga 600  
 ggtaactatg gccaaagatca atcctccatg agtagtggtg gtggcagtg ggccgggttat 660  
 ggcaactcaa accagagtgg tggagggtgg agcgggtggc atggacagca ggaccgtgga 720  
 ggcccgccga ggggtggcag tgggtggcgc ggccggcggc cgggtgggtg ttacacccgc 780  
 agcagtggtg gctatgaacc cagaggtcgt ggaggtggcc gtggaggcag aggtggcatg 840  
 ggccgaagtg accgtgggtg cttcaataaa ttggtggcc ctccgggacca aggtacagt 900  
 catgactccg acacaggataa ttcagacaaa aacacacatc ttgtgcaagg cgtgggtgag 960  
 aatgttacaa ttgagctcgt ggctgattac ttcaagcaga ttggtattat taagacaaac 1020  
 aagaaaaagg gacagcccat gattaatttg tacacagaca gggaaactgg accgtggaag 1080  
 ggagaggcaa cgggtctctt tgatgaccca ccttcagcta aagcagctat tgactggttt 1140  
 gggtgtaaag aattctccgg aaatcctatc aaggtctcat ttgctactgc ccgggcagac 1200  
 ttaactcggg gtggtggcaa tggctgtgga ggcgagggc gaggaggacc catgggcccgt 1260  
 ggaggtgatg gagggtgggt cagtggtggt ggtggccgag gaggatttcc cagtgagggt 1320  
 ggtggcgggt gaggacagca ggcagctggt gactggaagt gtcttaatcc cactgtgtag 1380  
 aatatgaact tctcttgtag gaatgaatgc aaccagtgtg aggccctcaa accagatggc 1440  
 ccaggagggg gaccaggtgg ctctcacatg gggggtaact acggggatga tctgtgtggt 1500  
 ggcagagggg gctatgatcg aggcggctac cggggccgcg gcggggaccg tggagggttc 1560  
 cgagggggccc ggggtgggtg ggacagaggt ggccttggcc ctggcgaagt ggattccagg 1620  
 ggtgagcaca gacaggtatg caggagaggc cgtattaat tagcctggct cccaggttcc 1680  
 tggaaacagt ttttgtctcg taccagtggt tacctcgttt attttgtaac cttccaattc 1740  
 ctgatacccc aagggttttt tttgtgtcgg actatgtaat tgtaactata cctctggttc 1800  
 ccattaaaag tgaccatttt agtt 1824

<210> 180  
 <211> 195  
 <212> PRT  
 <213> Homo sapiens

<400> 180  
 Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser Tyr Pro Gly Tyr  
 1 5 10 15  
 Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser Tyr Gly Ser Ser  
 20 25 30  
 Ser Gln Ser Tyr Gly Gln Pro Gln Ser Gly Ser Tyr Ser Gln  
 35 40 45  
 Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly Gln Gln Gln Ser  
 50 55 60

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Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln Tyr Asn Ser Ser  
 65 70 75 80  
 Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn Tyr Gly Gln Asp  
 85 90 95  
 Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly Gly Tyr Gly Asn  
 100 105 110  
 Gln Asp Gln Ser Gly Gly Gly Gly Ser Gly Gly Tyr Gly Gln Gln Asp  
 115 120 125  
 Arg Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly Gly Ala Ala Ala  
 130 135 140  
 Val Val Val Thr Thr Ala Ala Val Val Ala Met Asn Pro Glu Val Val  
 145 150 155 160  
 Glu Val Ala Val Glu Ala Glu Val Ala Trp Ala Glu Val Thr Val Val  
 165 170 175  
 Ala Ser Ile Asn Leu Val Cys Ser Arg Arg Lys Cys Ile Phe Ile His  
 180 185 190  
 His His Ser  
 195

&lt;210&gt; 181

&lt;211&gt; 652

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 181

cagagctccc aatcgtctta cgggcagcag tcctcctacc ctggctatgg ccagcagcca 60  
 gctcccagca gcacctcggg aagttacggt agcagttctc agagcagcag ctatgggcag 120  
 cccagcagtg ggagctacag ccagcagcct agctatgggt gacagcagca aagctatgga 180  
 cagcagcaaa gctataatcc ccctcagggc tatggacagc agaaccagta caacagcagc 240  
 agtggtgggt gagggtggag tggaggtgga ggtaactatg gccaaagatca atctcccatg 300  
 agtagtgggt gtggcagtg tggcggttat ggcaatcaag accagagtggt tggaggtggc 360  
 agcgggtggct atggacagca ggaccgtgga ggcgcgcgga ggggtggcag tgggtggcggc 420  
 ggggcggcgg cggtgggtgt tacaaccgca gcagtgtgtg ctatgaaccc agaggtcgtg 480  
 gaggtggcgg tggaggcaga ggtggcatgg gcggaagtga ccgtgggtggc ttcaataaat 540  
 ttggtgtgtt caagaaggaa gtgtatcttc atacatcacc actcctgaaa gcagatgtgc 600  
 ttttcagac tgatccaact gcagagatgg cagctgagtc attgcctttc tc 652

&lt;210&gt; 182

&lt;211&gt; 462

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 182

Met Ala Ser Asn Asp Tyr Thr Gln Gln Ala Thr Gln Ser Tyr Gly Ala  
 1 5 10 15  
 Tyr Pro Thr Gln Pro Gly Gln Gly Tyr Ser Gln Gln Ser Ser Gln Pro  
 20 25 30

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Tyr Gly Gln Gln Ser Tyr Ser Gly Tyr Ser Gln Ser Thr Asp Thr Ser  
 35 40 45  
 Gly Tyr Gly Gln Ser Ser Tyr Ser Ser Tyr Gly Gln Ser Gln Asn Thr  
 50 55 60  
 Gly Tyr Gly Thr Gln Ser Thr Pro Gln Gly Tyr Gly Ser Thr Gly Gly  
 65 70 75 80  
 Tyr Gly Ser Ser Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser  
 85 90 95  
 Tyr Pro Gly Tyr Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser  
 100 105 110  
 Tyr Gly Ser Ser Ser Gln Ser Ser Ser Tyr Gly Gln Pro Gln Ser Gly  
 115 120 125  
 Ser Tyr Ser Gln Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly  
 130 135 140  
 Gln Gln Gln Ser Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln  
 145 150 155 160  
 Tyr Asn Ser Ser Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn  
 165 170 175  
 Tyr Gly Gln Asp Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly  
 180 185 190  
 Gly Tyr Gly Asn Gln Asp Gln Ser Gly Gly Gly Gly Ser Gly Gly Tyr  
 195 200 205  
 Gly Gln Gln Asp Arg Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly Gly  
 210 215 220  
 Gly Gly Gly Gly Gly Gly Gly Tyr Asn Arg Ser Ser Gly Gly Tyr Glu  
 225 230 235 240  
 Pro Arg Gly Arg Gly Gly Gly Arg Gly Gly Arg Gly Gly Met Gly Gly  
 245 250 255  
 Ser Asp Arg Gly Gly Phe Asn Lys Phe Gly Val Phe Lys Lys Glu Val  
 260 265 270  
 Tyr Leu His Thr Ser Pro His Leu Lys Ala Asp Val Leu Phe Gln Thr  
 275 280 285  
 Asp Pro Thr Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser Phe Gly  
 290 295 300  
 Thr Leu Ser Ser Trp Glu Leu Glu Ala Trp Tyr Glu Asp Leu Gln Glu  
 305 310 315 320  
 Val Leu Ser Ser Asp Glu Asn Gly Gly Thr Tyr Val Ser Pro Pro Gly  
 325 330 335

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Asn Glu Glu Glu Glu Ser Lys Ile Phe Thr Thr Leu Asp Pro Ala Ser
   340                               345                               350

Leu Ala Trp Leu Thr Glu Glu Glu Pro Glu Pro Ala Glu Val Thr Ser
   355                               360                               365

Thr Ser Gln Ser Pro His Ser Pro Asp Ser Ser Gln Ser Ser Leu Ala
   370                               375                               380

Gln Glu Glu Glu Glu Glu Asp Gln Gly Arg Thr Arg Lys Arg Lys Gln
   385                               390                               395                               400

Ser Gly His Ser Pro Ala Arg Ala Gly Lys Gln Arg Met Lys Glu Lys
   405                               410                               415

Glu Gln Glu Asn Glu Arg Lys Val Ala Gln Leu Ala Glu Glu Asn Glu
   420                               425                               430

Arg Leu Lys Lys Gln Glu Ile Glu Arg Leu Thr Arg Glu Val Glu Ala Thr
   435                               440                               445

Arg Arg Ala Leu Ile Asp Arg Met Val Asn Leu His Gln Ala
   450                               455                               460

<210> 183
<211> 1678
<212> DNA
<213> Homo sapiens

<400> 183
gcggccgctg  tcgggtgtcga  gcgggtgttgg  aacttcgttg  cttgcttgcc  tgtgcgcgcg  50
tgccgcggaca  tggcctcaaa  cgattatacc  caacaagcaa  cccaaagcta  tggggccctac  120
cccaccacagc  ccgggcaggg  ctattcccag  cagagcagtc  agccctacgg  acagcagagt  180
tacagtggtt  atagccagtc  cacggacact  tcaggctatg  gccagagcag  ctattctctt  240
tatggccaga  gccagaacac  aggctatgga  actcagtcga  ctcccaggg  atatgggtcg  300
actggcggtt  atggcagtag  ccagagctcc  caatcgtctt  accgggcagca  gtctctctac  360
cctggctatg  gccagcagcc  agctccacgc  agcacctcgg  gaagttaagg  tagcagttct  420
cagagcagca  gctatgggca  gccccagagt  gggagctaca  gccagcagcc  tagctatggt  480
ggcagcagcg  aaagctatgg  acagcagcaa  agctataatc  ccctcaggg  ctatggacag  540
cagaaccagt  acaacagcag  cagtggtggt  ggaggtggag  gtggaggtgg  aggtaacatc  600
ggccaagatc  aatcctccat  gagttagtgt  ggtggcagtg  gtggcggtta  tgggcaatcaa  660
gaccagagtg  gtggaggtgg  cagcgggtgg  tatggacagc  aggaccgtgg  aggcgcggcg  720
aggggtggca  gtggtggcgg  cggcggcgcg  ggcggtggtg  gttacaaccg  cagcagtggt  780
ggctatgaac  ccagaggtcg  tggaggtggc  cgtggaggca  gagtggtgat  gggcggaagt  840
gaccgtggtg  gcttcaataa  atttggtgtg  ttcaagaagg  aagtgtatct  tcatacatca  900
ccacacatga  aagcagatgt  gcttttccag  actgatccaa  ctgcagagat  ggcagctgag  960
tcattgcctt  tctccttcgg  gacactgtcc  agctgggagc  tggaaagcct  gtatgaggac  1020
ctgcaagagg  tctgtcttcc  agatgaaaat  gggggtacct  atgtttcacc  tctctggaat  1080
gaagagggaag  aatcaaaaat  cttcacacct  cttgacccgt  cttctctggc  ttggctgact  1140
gagaggagcg  cagaaccagc  agaggtcaca  agcacctccc  agagccctca  ctctccagat  1200
tccagtcaga  gctccctggc  tcaggaggaa  gaggaggaa  accaagggag  aaccaggaaa  1260
cggaaacaga  gtggtcattc  cccagccggg  gctggaaagg  agcgcatgaa  ggagaaagaa  1320
caggagaagt  aaaggaaagt  gccacagcta  gctgaagaga  atgaacggat  caagcaggaa  1380
atcgagcgcc  tgaccaggga  agtagaggcg  actgcggcag  ctctgatgga  ccgaatgggt  1440
aatctgcacc  aagcatgaac  aattgggagc  atcagtcgcc  cacttgggce  acactaccga  1500
cctttccacg  aagtgggtac  tgactaccct  ctactagtg  ccaatgatgt  gacctccaat  1560
cccacatacg  caggggggaag  gcttgaggta  gacaaaagga  aaggtctcag  cttgtatata  1620

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gagattgtac atttatttat tactgtccct atctattaaa gtgactttct atgaaaaa 1678

&lt;210&gt; 184

&lt;211&gt; 525

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 184

Met Ala Ser Asn Asp Tyr Thr Gln Gln Ala Thr Gln Ser Tyr Gly Ala  
 1 5 10 15

Tyr Pro Thr Gln Pro Gly Gln Gly Tyr Ser Gln Gln Ser Ser Gln Pro  
 20 25 30

Tyr Gly Gln Gln Ser Tyr Ser Gly Tyr Ser Gln Ser Thr Asp Thr Ser  
 35 40 45

Gly Tyr Gly Gln Ser Ser Tyr Ser Ser Tyr Gly Gln Ser Gln Asn Ser  
 50 55 60

Tyr Gly Thr Gln Ser Thr Pro Gln Gly Tyr Gly Ser Thr Gly Gly Tyr  
 65 70 75 80

Gly Ser Ser Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser Tyr  
 85 90 95

Pro Gly Tyr Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser Tyr  
 100 105 110

Gly Ser Ser Ser Gln Ser Ser Ser Tyr Gly Gln Pro Gln Ser Gly Ser  
 115 120 125

Tyr Ser Gln Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly Gln  
 130 135 140

Gln Gln Ser Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln Tyr  
 145 150 155 160

Asn Ser Ser Ser Gly Gly Gly Gly Gly Gly Gly Gly Gly Gly Asn Tyr  
 165 170 175

Gly Gln Asp Gln Ser Ser Met Ser Ser Gly Gly Gly Ser Gly Gly Gly  
 180 185 190

Tyr Gly Asn Gln Asp Gln Ser Gly Gly Gly Ser Gly Gly Tyr Gly  
 195 200 205

Gln Gln Asp Arg Gly Gly Arg Gly Arg Gly Gly Ser Gly Gly Gly Gly  
 210 215 220

Gly Gly Gly Gly Gly Gly Tyr Asn Arg Ser Ser Gly Gly Tyr Glu Pro  
 225 230 235 240

Arg Gly Arg Gly Gly Gly Arg Gly Gly Arg Gly Gly Met Gly Gly Ser  
 245 250 255

Asp Arg Gly Gly Phe Asn Lys Phe Gly Gly Pro Arg Asp Gln Gly Ser

139/299

260	265	270
Arg His Asp Ser Glu Gln Asp Asn Ser Asp Asn Asn Thr Ile Phe Val		
275	280	285
Gln Gly Leu Gly Glu Asn Val Thr Ile Glu Ser Val Ala Asp Tyr Phe		
290	295	300
Lys Gln Ile Gly Ile Ile Lys Thr Asn Lys Lys Thr Gly Gln Pro Met		
305	310	315
Ile Asn Leu Tyr Thr Asp Arg Glu Thr Gly Lys Leu Lys Gly Glu Ala		
325	330	335
Thr Val Ser Phe Asp Asp Pro Pro Ser Ala Lys Ala Ala Ile Asp Trp		
340	345	350
Phe Asp Gly Lys Glu Phe Ser Gly Asn Pro Ile Lys Val Ser Phe Ala		
355	360	365
Thr Arg Arg Ala Asp Phe Asn Arg Gly Gly Gly Asn Gly Arg Gly Gly		
370	375	380
Arg Gly Arg Gly Gly Pro Met Gly Arg Gly Gly Tyr Gly Gly Gly Gly		
385	390	395
Ser Gly Gly Gly Gly Arg Gly Gly Phe Pro Ser Gly Gly Gly Gly Gly		
405	410	415
Gly Gly Gln Gln Arg Ala Gly Asp Trp Lys Cys Pro Asn Pro Thr Cys		
420	425	430
Glu Asn Met Asn Phe Ser Trp Arg Asn Glu Cys Asn Gln Cys Lys Ala		
435	440	445
Pro Lys Pro Asp Gly Pro Gly Gly Gly Pro Gly Gly Ser His Met Gly		
450	455	460
Gly Asn Tyr Gly Asp Asp Arg Arg Gly Gly Arg Gly Gly Tyr Asp Arg		
465	470	475
Gly Gly Tyr Arg Gly Arg Gly Gly Asp Arg Gly Gly Phe Arg Gly Gly		
485	490	495
Arg Gly Gly Gly Asp Arg Gly Gly Phe Gly Pro Gly Lys Met Asp Ser		
500	505	510
Arg Gly Glu His Arg Gln Asp Arg Arg Glu Arg Pro Tyr		
515	520	525

&lt;210&gt; 185

&lt;211&gt; 1822

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 185

gcggccgctg gcgtcgggtg tcagcgggtg tggaaacttgc ttgcttgctt gctgtgogc 60

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```

gcgtgcgccg acatggcctc aaacgattat acccaacaag caaccctaaag ctatggggcc 120
taccacaccc agccggggca gggctattcc cagcagagca gtcagcccta cggacagcag 180
agttacagtg gttatagcca gtccacggac acttcaggct atggccagag cagctattct 240
tcttatggcc agagccagaa cagctatgga actcagtcga ctccccaggg atatggctcg 300
actggcggtc atggcagtag ccagagctcc caatcgcttt acgggcagca gtccctctat 360
cctggctatg gccacgagcc agctcccgag agcacctcgg gaagttaacg tagcagttct 420
cagagcagca gctatgggca gccccagagt gggagctaca gccagcagcc tagctatggt 480
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cagaaccagt acaacagcag cagtgtgtgt ggaggtggag gtggaggtgg aggttaactat 600
ggccaagatc aatcctccat gagttagtgt ggtggcagtg gtggcggtta tggcaatcaa 660
gaccagagtg gtggaggtgg cagcgggtggc tatggacagc aggaccgtgg aggcgcgggc 720
aggggtggca gtgtgtggcg cggcggtggc ggcggtgtgt gttacaacgg cagcagtggt 780
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tttttgcctc gtaccagtg ttaccctcgt tattttgtta ccttccaatt cctgatcacc 1740
caagggtttt ttgtgtcgg actatgtaat tgtactata cctctgggtc ccattaaaag 1800
tgaccatttt agtataaaaa aa 1822

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&lt;210&gt; 186

&lt;211&gt; 120

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 186

```

tgggtttctaa agatgaaatt aagaattggt ccacaagggt taagtgtctg gtggtaaaagt 60
tgggctcgga ggctacagat aaccctaaata taagtggcac ggagaaagct aaagcagaga 120

```

&lt;210&gt; 187

&lt;211&gt; 118

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 187

```

tgagtggtg ggagacaact ccgaatgttt aattctggaa gagggatgta acattgccct 60
gaggattcga gatggtagtg aattgatcta gattggaac aatggaatta gaagtgtt 118

```

&lt;210&gt; 188

&lt;211&gt; 120

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 188

141/299

gtgtggggaga caactccgaa tgtttaattc tgggaagagg atgtaacatt gccttgagga 60  
 tggtggctca cacctgtaat cccagcactt tgggagacca gaggtgggtg gatcacctg 120

<210> 189  
 <211> 126  
 <212> PRT  
 <213> Homo sapiens

<400> 189  
 Gln Ser Ser Gln Ser Ser Tyr Gly Gln Gln Ser Ser Tyr Pro Gly Tyr  
 1 5 10 15  
 Gly Gln Gln Pro Ala Pro Ser Ser Thr Ser Gly Ser Tyr Gly Ser Ser  
 20 25 30  
 Ser Gln Ser Ser Ser Tyr Gly Gln Pro Gln Ser Gly Ser Tyr Ser Gln  
 35 40 45  
 Gln Pro Ser Tyr Gly Gly Gln Gln Gln Ser Tyr Gly Gln Gln Gln Ser  
 50 55 60  
 Tyr Asn Pro Pro Gln Gly Tyr Gly Gln Gln Asn Gln Tyr Asn Ser Ser  
 65 70 75 80  
 Ser Gly Gly Gly Gly Gly Gly Gly Gly Val Phe Lys Lys Glu Val  
 85 90 95  
 Tyr Leu His Thr Ser Pro Leu Leu Lys Ala Asp Val Leu Phe Gln Thr  
 100 105 110  
 Asp Pro Thr Ala Glu Met Ala Ala Glu Ser Leu Pro Phe Ser  
 115 120 125

<210> 190  
 <211> 377  
 <212> DNA  
 <213> Homo sapiens

<400> 190  
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 gctcccagca gcacctcggg aagttacggt agcagttctc agagcagcag ctatggggcag 120  
 cccagagtg ggagctacag ccagcagcct agctatgggt gacagcagca aagctatgga 180  
 cagcagcaaaa gctataatcc cctcagggc tatggacagc agaaccagta caacagcagc 240  
 agtggtgggt gaggtggagg tggaggtgga gtgttcaaga aggaagtgta tcttcataca 300  
 tcaccactcc tgaagcaga tgtgcttttc cagactgac caactgcaga gatggcagct 360  
 gagtcatgac cttttc 377

<210> 191  
 <211> 689  
 <212> PRT  
 <213> Homo sapiens

<400> 191  
 Pro Ser Val Ser Ser Ile Ser Arg Ile Leu Arg Ser Lys Phe Gly Lys  
 1 5 10 15

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Gly Glu Glu Glu Glu Ala Asp Leu Glu Arg Lys Glu Ala Glu Glu Ser  
                     20                                    25                                    30

Glu Lys Lys Ala Lys His Ser Ile Asp Gly Ile Leu Ser Glu Arg Ala  
                     35                                    40                                    45

Ser Ala Pro Gln Ser Asp Glu Gly Ser Asp Ile Asp Ser Glu Pro Asp  
                     50                                    55                                    60

Leu Pro Leu Lys Arg Lys Gln Arg Arg Ser Arg Thr Thr Phe Thr Ala  
                     65                                    70                                    75                                    80

Glu Gln Leu Glu Glu Leu Glu His Val Ala Phe Glu Arg Thr His Tyr  
                     85                                    90                                    95

Pro Asp Ile Tyr Thr Arg Glu Glu Leu Ala Gln Arg Ala Lys Leu Thr  
                     100                                    105                                    110

Glu Ala Arg Val Gln Val Trp Phe Ser Asn Arg Arg Ala Arg Trp Arg  
                     115                                    120                                    125

Lys Gln Ala Gly Ala Asn Gln Leu Met Ala Phe Asn His Leu Ile Pro  
                     130                                    135                                    140

Gly Gly Phe Pro Pro Thr Ala Met Pro Thr Leu Pro Thr Tyr Gln Leu  
                     145                                    150                                    155                                    160

Ser Glu His Ser Tyr Gln Pro Thr Ser Ile Pro Gln Ala Val Ser Asp  
                     165                                    170                                    175

Pro Ser Ser Thr Val His Arg Pro Gln Pro Leu Pro Pro Ser Thr Val  
                     180                                    185                                    190

His Gln Ser Thr Ile Pro Ser Asn Pro Asp Ser Ser Ser Ala Tyr Cys  
                     195                                    200                                    205

Leu Pro Ser Thr Arg His Gly Phe Ser Ser Tyr Thr Asp Ser Phe Val  
                     210                                    215                                    220

Pro Pro Ser Gly Pro Ser Asn Pro Met Asn Pro Thr Ile Gly Asn Gly  
                     225                                    230                                    235                                    240

Leu Ser Pro Gln Asn Ser Ile Arg His Asn Leu Ser Leu His Ser Lys  
                     245                                    250                                    255

Phe Ile Arg Val Gln Asn Glu Gly Thr Gly Lys Ser Ser Trp Trp Met  
                     260                                    265                                    270

Leu Asn Pro Glu Gly Gly Lys Ser Gly Lys Ser Pro Arg Arg Arg Ala  
                     275                                    280                                    285

Ala Ser Met Asp Asn Asn Ser Lys Phe Ala Lys Ser Arg Ser Arg Ala  
                     290                                    295                                    300

Ala Lys Lys Lys Ala Ser Leu Gln Ser Gly Gln Glu Gly Ala Gly Asp  
                     305                                    310                                    315                                    320

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Ser Pro Gly Ser Gln Phe Ser Lys Trp Pro Ala Ser Pro Gly Ser His  
 325 330 335  
 Ser Asn Asp Asp Phe Asp Asn Trp Ser Thr Phe Arg Pro Arg Thr Ser  
 340 345 350  
 Ser Asn Ala Ser Thr Ile Ser Gly Arg Leu Ser Pro Ile Met Thr Glu  
 355 360 365  
 Gln Asp Asp Leu Gly Glu Gly Asp Val His Ser Met Val Tyr Pro Pro  
 370 375 380  
 Ser Ala Ala Lys Met Ala Ser Thr Leu Pro Ser Leu Ser Glu Ile Ser  
 385 390 395 400  
 Asn Pro Glu Asn Met Glu Asn Leu Leu Asp Asn Leu Asn Leu Leu Ser  
 405 410 415  
 Ser Pro Thr Ser Leu Thr Val Ser Thr Gln Ser Ser Pro Gly Thr Met  
 420 425 430  
 Met Gln Gln Thr Pro Cys Tyr Ser Phe Ala Pro Pro Asn Thr Ser Leu  
 435 440 445  
 Asn Ser Pro Ser Pro Asn Tyr Gln Lys Tyr Thr Tyr Gly Gln Ser Ser  
 450 455 460  
 Met Ser Pro Leu Pro Gln Met Pro Ile Gln Thr Leu Gln Asp Asn Lys  
 465 470 475 480  
 Ser Ser Tyr Gly Gly Met Ser Gln Tyr Asn Cys Ala Pro Gly Leu Leu  
 485 490 495  
 Lys Glu Leu Leu Thr Ser Asp Ser Pro Pro His Asn Asp Ile Met Thr  
 500 505 510  
 Pro Val Asp Pro Gly Val Ala Gln Pro Asn Ser Arg Val Leu Gly Gln  
 515 520 525  
 Asn Val Met Met Gly Pro Asn Ser Val Met Ser Thr Tyr Gly Ser Gln  
 530 535 540  
 Ala Ser His Asn Lys Met Met Asn Pro Ser Ser His Thr His Pro Gly  
 545 550 555 560  
 His Ala Gln Gln Thr Ser Ala Val Asn Gly Arg Pro Leu Pro His Thr  
 565 570 575  
 Val Ser Thr Met Pro His Thr Ser Gly Met Asn Arg Leu Thr Gln Val  
 580 585 590  
 Lys Thr Pro Val Gln Val Pro Leu Pro His Pro Met Gln Met Ser Ala  
 595 600 605  
 Leu Gly Gly Tyr Ser Ser Val Ser Ser Cys Asn Gly Tyr Gly Arg Met  
 610 615 620  
 Gly Leu Leu His Gln Glu Lys Leu Pro Ser Asp Leu Asp Gly Met Phe

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625	630	635	640
Ile Glu Arg Leu Asp Cys Asp Met Glu Ser Ile Ile Arg Asn Asp Leu			
645	650	655	
Met Asp Gly Asp Thr Leu Asp Phe Asn Phe Asp Asn Val Leu Pro Asn			
660	665	670	
Gln Ser Phe Pro His Ser Val Lys Thr Thr Thr His Ser Trp Val Ser			
675	680	685	

Gly

&lt;210&gt; 192

&lt;211&gt; 3517

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 192

```

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gaggccgactg tggagaggaa ggaggcagag gaaagcgaga agaaggccaa acacagcatc 120
gagggcatccc tggagcagcg agcctcagca ccccaatcag atgaaggctc tatattgac 180
tctgaaccagc atttaccact aaagaggaaa cagcgcagaa gccgaaccac ctctcacaga 240
gaacagctgg aggaactgga gcacgttgct tttagagaaa ctccattacc tgacatttat 300
actaggggagg aactggccca gagggcgagg ctccaccgag cccgagtaca ggtctggttt 360
agcaaccgccg gtgcaagatg gaggaagcaa gctggggcca atcaactgat ggctttcaac 420
catctcatctc ccgggggatt cctccaccat gccatgcoga ccttgccaac gtaccagctg 480
tcggagcactc cttaccagcc cacatctatt ccacaagctg tgtcagatcc cagcagcacc 540
gttcacagac ctoaaccgct tcttccaagc actgtacacc aaagcacagt tcttccaac 600
ccagacagca gctctgccta ctgctctccc agccaccagg atggattttc cagctatata 660
gacagctttg tgcctcctgc ggggcctctc aaccccatga acccccatc atggcaatggc 720
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cagaatgaag gaactggaaa aagttcttgg tggatgctca atccagaggg tggcaagagc 840
gggaatctctc ctaggagaag agtgcctacc atggacaaca acagtaaat tgcctaagagc 900
cgaagccgag ctggccaagaa gaaagcatct ctccagctgt gccaggaggg tgcctggggc 960
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ttctcccttc tgccttcgag attagattac ttagcac 3517

```

&lt;210&gt; 193

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 193

```

Pro Tyr Gly Tyr Asp Gln Ser Pro Phe Met Cys Asn Lys Arg Ala Glu
  1             5             10             15

```

```

Asp Phe Gln Gly Asn Asp Leu Asp Asn Asp Pro Asn Arg Gly Asn Gln
      20             25             30

```

```

Val Glu Arg Pro Gln Met Thr Phe Gly Arg Leu Gln Gly Ile Ser Pro
      35             40             45

```

```

Lys Ile Met Pro Lys Lys Pro
      50             55

```

&lt;210&gt; 194

&lt;211&gt; 165

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 194

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ccttatggat atgaccagtc tcttttcatt tgtaataaac gggccgaaga cttccagggg 60
aatgatttgg ataagtaccc taacgtggg aatcagggtg aacgtctcca gatgactttc 120
ggcagggtcc agggaatctc ccggaagatc atgcccgaaga agcca 165

```

&lt;210&gt; 195

&lt;211&gt; 188

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



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&lt;400&gt; 195

```

Met Asn Gly Asp Asp Ala Phe Ala Arg Arg Pro Thr Val Gly Ala Gln
  1             5             10             15

Ile Pro Glu Lys Ile Gln Lys Ala Phe Asp Asp Ile Ala Lys Tyr Phe
          20             25             30

Ser Lys Glu Glu Trp Glu Lys Met Lys Ala Ser Glu Lys Ile Phe Tyr
      35             40             45

Val Tyr Met Lys Arg Lys Tyr Glu Ala Met Thr Lys Leu Gly Phe Lys
      50             55             60

Ala Thr Leu Pro Pro Phe Met Cys Asn Lys Arg Ala Glu Asp Phe Gln
      65             70             75             80

Gly Asn Asp Leu Asp Asn Asp Pro Asn Arg Gly Asn Gln Val Glu Arg
          85             90             95

Pro Gln Met Thr Phe Gly Arg Leu Gln Gly Ile Ser Pro Lys Ile Met
      100             105             110

Pro Lys Lys Pro Ala Glu Glu Gly Asn Asp Ser Glu Glu Val Pro Glu
      115             120             125

Ala Ser Gly Pro Gln Asn Asp Gly Lys Glu Leu Cys Pro Pro Gly Lys
      130             135             140

Pro Thr Thr Ser Glu Lys Ile His Glu Arg Ser Gly Pro Lys Arg Gly
      145             150             155             160

Glu His Ala Trp Thr His Arg Leu Arg Glu Arg Lys Gln Leu Val Ile
      165             170             175

Tyr Glu Glu Ile Ser Asp Pro Glu Glu Asp Asp Glu
      180             185

```

&lt;210&gt; 196

&lt;211&gt; 766

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 196

```

ctctctttcg attcttccat actcagagta ogcaoggtet gattttotet ttggattcct 60
ccaaaatacag agtcagactg ctcccggtgc catgaacgga gaocagcgcct ttgcaaggag 120
accacgggtt ggtgctcaaa taaccagagaa gatccaaaag gccttcgatg atattgccaa 180
atactctctc aaggaagagt gggaaaagat gaaagcctcg gagaataatc tctatgtgta 240
tatgaagaga aagtatgagg ctatgactaa actagggttc aaggccaccct tcccaccttt 300
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tgggaatcac gttgaacgtc ctccagatgac ttccggcagg ctccaggggaa tctccccgaa 420
gatcatgccc aagaagccag cagaggaagg aaatgattcg gaggaagtgc cagaagcatc 480
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gattcacgag agatctggac ccaaaagggg ggaacatgcc tggacccaca gactgcgtga 600
gagaaaaacag ctggtgattt atgaagagat cagcgaccct gaggaagatg acgagtaact 660
ccctcagagg atacgacaca tgcccatgat gagaagcaga acgtggtgac ctttcacgaa 720
catgggcatg gctgcggacc cctogtcac aggtgcatag caagtg 766

```

147/299

<210> 197  
 <211> 548  
 <212> DNA  
 <213> Homo sapiens

<400> 197  
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gagttttacg	aaaaaatatt	tataacgac	tcttttaaaa	gatctatgtc	ttgaaaatag	9180
agaagagaaca	cagggtctggc	cagggaactg	ctgcaattgg	tgcagttttg	aatgcaaacat	9240
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tttctatgac	ttttaggtag	gatgagagca	gaaggtagat	cctaaaaagc	atggtgagag	9360
gatcaaatgt	ttttatatac	acatcttcta	ttatttgatt	actttgagtt	aaacagtggt	9420
ttagtgtatg	atttttctat	tcttttctct	tgacgtttac	tttcaagtaa	cacaaactct	9480
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aacctatctc	ccaaagcatt	aatatccaat	catgctcggt	atgttttaac	cagcagaagc	9600
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catgttctcc	tccaagctac	tttaataaag	gatcttataa	tgggcaggag	gactgtgaac	9720
aagacacctc	ataataaggt	tgatgtctga	agtagcaaat	ctcttggaac	cgcaaacctc	9780
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ctccccaaag	tatatatact	atataagaga	gttgtagaca	aacagaatga	taaagctggt	10020
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aacacagggt	ttcaaggcca	gcctggggcaa	cataacaaga	tctgtctctc	caaaaaaaaa	10140
aaaaaaaaaa	agaaaagagag	aggggccggcg	gtggtggctc	acgcctgtaa	tccagcaact	10200
ttggggagcc	gagccggggcg	gatcacctgt	ggctcaggagt	ttgagaccag	ctcgcccaac	10260
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tgtaatccca	gcgcttgagg	aggctgaggc	aggagaatcg	cttgaaccca	ggaggtggag	10380
gttgacgtta	gctgagatcg	tgccgttgca	ctccagcctg	ggcgacaaga	gcaggaactct	10440
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aggaatggga	agcatttgcaa	ggaaatttgt	ctttatccaa	caaaatgtaa	ggagccaata	10560
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aagatgagca	gatccacagg	aaaacttgaa	tgcaacaact	tcttatttta	atcttatattg	10740
acataagatt	gtaaaagatt	taaaatttgt	tacttcatgt	atttttttat	atttttatatt	10800
attttgcgtc	tatatgattt	tattatacat	gatttctctt	tctgatata	tgaatggag	10860
tctcaaggt	tcataaattt	ataactttag	aaatgattct	ataacaacog	tatgtaattg	10920
taacatttga	gtaattgtgc	tacgaagcca	tttctcttga	tttttagtaa	acttttatga	10980
cagcaaatgt	gctctctgct	cactttcaat	cagtttaata	aatgataaat	atttttgtaa	11040
gctgtgaaga	taaaatacca	ataaaaataa	tataaaagt	atttataatga	agttaaaata	11100
aaaaatcagt	atgatggagt	aaacttgaga	gtccagaagt	tatcccatac	atctgtaatc	11160
aactaatttc	gtcaagggt	gtcaaggcca	ttcaatggag	aaaa		11204

&lt;210&gt; 202

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 202

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```

Met Asp Ser Leu Leu Met Asn Arg Arg Lys Phe Leu Tyr Gln Phe Lys
 1           5           10           15

Asn Val Arg Trp Ala Lys Gly Arg Arg Glu Thr Tyr Leu Cys Tyr Val
          20           25           30

Val Lys Arg Arg Asp Ser Ala Thr Ser Phe Ser Leu Asp Phe Gly Tyr
          35           40           45

Leu Arg Asn Lys Asn Gly Cys His Val Glu Leu Leu Phe Leu Arg Tyr
 50           55           60

Ile Ser Asp Trp Asp Leu Asp Pro Gly Arg Cys Tyr Arg Val Thr Trp
 65           70           75           80

Phe Thr Ser Trp Ser Pro Cys Tyr Asp Cys Ala Arg His Val Ala Asp
          85           90           95

Phe Leu Arg Gly Asn Pro Asn Leu Ser Leu Arg Ile Phe Thr Ala Arg
          100          105          110

Leu Tyr Phe Cys Glu Asp Arg Lys Ala Glu Pro Glu Gly Leu Arg Arg
          115          120          125

Leu His Arg Ala Gly Val Gln Ile Ala Ile Met Thr Phe Lys Asp Tyr
          130          135          140

Phe Tyr Cys Trp Asn Thr Phe Val Glu Asn His Glu Arg Thr Phe Lys
          145          150          155          160

Ala Trp Glu Gly Leu His Glu Asn Ser Val Arg Leu Ser Arg Gln Leu
          165          170          175

Arg Arg Ile Leu Leu Pro Leu Tyr Glu Val Asp Asp Leu Arg Asp Ala
          180          185          190

Phe Arg Thr Leu Gly Leu
          195

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&lt;210&gt; 203

&lt;211&gt; 2791

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 203

```

gaaccatcat taattgaagt gagatttttc tggcctgaga cttgcaggga ggcaagaaga 60
cactctggac accactatgg acagcctctt gatgaaccgg aggaagtttc tttaaccaatt 120
caaaaatgtc cgctgggcta agggctcggcg tgagacctac ctgtgctaag tagtgaagag 180
gogtgacagt gctacatcct ttctactgga ctttggttat cttcgcaata agaaccggctg 240
ccacgtggaa ttgctcttcc tccgctacat ctoggactgg gacctagacc ctggccgcctg 300
ctaccggctc acctgggttca cctcctggag cccctgctac gactgtgccc gacatgtggc 360
cgactttctg cgagggaacc ccaacctcag tctgaggatc ttcaccgcgc gccctactt 420
ctgtgaggac cgcaaggctg agcccgaggg gctgcggcgg ctgcacgcgc cgggggtgca 480
aatagccatc atgaccttca aagattattt ttactgtcgg aatacttttg tagaaaacca 540
tgaaagaact ttcaagcctt ggggaaggct gcataaaaat tcagttctgc tctccagaca 600
gcttcggcgc atccttttgc cctgtatga ggttgatgac ttacgagacg catttctac 660
tttgggactt tgatagcaac ttccaggaat gtcacacacg atgaaatc atctgtgaag 720

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acagtggata aaaaacagtc cttcaagtct tctctgtttt tattcttcaa ctctcacttt 780
cttagagttt acagaaaaaa tatttatata cgactcttta aaaagatcta tgccttgaaa 840
atagagaagg aaacacaggtc tggccaggga cgtgctgcaa ttggtgcagt ttggaatgca 900
acattgtccc ctactgggaa taacagaact gcaggacctg ggcagcatctt aaagtgtcaa 960
cgtttttcta tgacttttag gtaggatgag agcagaaggt agatcctaaa aagcatgggt 1020
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gggtttagtg atagattttt ctattctttt cccttgacgt ttactttcaa gtacacaaaa 1140
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cccaactcat ctctccaaag cattaatatc caatcatgag ctgtatgttt taatcagcag 1260
aagcatgttt ttatgtttgt acaaaaagaag attgttatgg gtggggatgg aggtatagac 1320
catgcattgt ccacttcaag ctactttaat aaagatctt aaatgggca ggaggactgt 1380
gaacaagaca ccttaataat gggttgatgt ctgaagtagc aaatcttctg gaaacgcaaa 1440
ctcttttaag gaagtcccta atttagaaac acccacaac ttcacatatc ataattagca 1500
aacaattgga aggaagtgtg ttgaatgttg gggagaggaa aatctatggg ctctcgtggg 1560
tctcttcac tcagaaatgc caatcaggctc aaggtttgct acatttttga ttgtgtgtgat 1620
gcttctccca aaggtatat taaactataa gagagttgtg acaaaacaga atgataaagc 1680
tgccaacctg ggcaacgct catagttcta gctgcttggg aggttgagga gggaggtatg 1740
cttgaacaca ggtgttcaag gccagcctgg gcaacataac aagatcctgt ctctcaaaaa 1800
aaaaaaaaaa aaaaagaag agagagggcc gggcgtgtgt gctcacgctt gtaatccagc 1860
cactttggga ggcagagccg ggcggtcac ctgtggtcag gagtttgaga ccagcctggc 1920
caacatggca aaacccgctc tgtactcaaa atgcaaaaat tagccagggc tggtagcagg 1980
cacctgtaac ccacgtact tgggagggct aggcaggaga atcgcttgaa cccaggagggt 2040
ggaggttgca gtaagctgag atcggtccgt tgcactccag cctggggcagc agagcaga 2100
ctctgctcta gaaaaaaa aaaaaaagag agagagagag aaagagaaca atatttgga 2160
gagaaggatg ggaagcatt gcaaggaaat ttgtctttat tgcacaaaaa cttaaggagcc 2220
aataagggat cctatttgt ctcttttggt gtctatttgt ccttaacaac tgcttttgac 2280
agtgaagaaa atattcagaa taaccatct cctgtgcctg tattacctga cacccttgc 2340
aatgaagatg agcagatcca caggaaaaat tgaatgcaca actgtcttat ttaatactta 2400
ttgtacataa gtttgtaaaa gagttaaaaa ttgttaactc atgtattcat ttatatctta 2460
tattattttc cgtctaatga ttttttatta acatgatttc cttttctgat atattgaaat 2520
ggagcttcaa agcttcataa atttataact tttagaaatga ttctaataac aacgtatgta 2580
attgtaacat tgcagtaatg gtgctacgaa gccatttctc ttgattttta gtaaaacttt 2640
atgacagcaa atttctcttc ggtcactctt caatcagtta aataaatgat aaataatttt 2700
ggaagcttgg aagataaaaat accaaataaa ataataaaa agtgatttat atgaagttaa 2760
aataaaaaat cagtatgatg gaataaactt g' 2791

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&lt;210&gt; 204

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 204

Met Asp Ser Leu Leu Met Asn Arg Arg Lys Phe Leu Tyr Gln Phe Lys

1

5

10

15

Asn Val Arg Trp Ala Lys Gly Arg Arg Glu Thr Tyr Leu Cys Tyr Val

20

25

30

Val Lys Arg Arg Asp Ser Ala Thr Ser Phe Ser Leu Asp Phe Gly Tyr

35

40

45

Leu Arg Asn Lys Asn Gly Cys His Val Glu Leu Leu Phe Leu Arg Tyr

50

55

60

Ile Ser Asp Trp Asp Leu Asp Pro Gly Arg Cys Tyr Arg Val Thr Trp

65

70

75

80

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Phe Thr Ser Trp Ser Pro Cys Tyr Asp Cys Ala Arg His Val Ala Asp  
                   85                  90                  95  
 Phe Leu Arg Gly Asn Pro Asn Leu Ser Leu Arg Ile Phe Thr Ala Arg  
                   100                  105                  110  
 Leu Tyr Phe Cys Glu Asp Arg Lys Ala Glu Pro Glu Gly Leu Arg Arg  
                   115                  120                  125  
 Leu His Arg Ala Gly Val Gln Ile Ala Ile Met Thr Phe Lys Asp Tyr  
                   130                  135                  140  
 Phe Tyr Cys Trp Asn Thr Phe Val Glu Asn His Glu Arg Thr Phe Lys  
                   145                  150                  155                  160  
 Ala Trp Glu Gly Leu His Glu Asn Ser Val Arg Leu Ser Arg Gln Leu  
                   165                  170                  175  
 Arg Arg Ile Leu Leu Pro Leu Tyr Glu Val Asp Asp Leu Arg Asp Ala  
                   180                  185                  190  
 Phe Arg Thr Leu Gly Leu  
                   195

&lt;210&gt; 205

&lt;211&gt; 2791

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 205

gaaccatcat taattgaagt gagatttttc tggcctgaga cttgcaggga ggcaagaaga 60  
 cactctggac accactatgg acagcctctt gatgaaccgg aggaagtttc tttaaccaatt 120  
 caaaaaatgtc cgctgggcta agggctcggc tgagacctac ctgtgctaag tagtgaagag 180  
 gcgtgacagt gctacatcct ttctactgga ctttggttat cttcgcaata agaaccggctg 240  
 ccacgtggaa ttgctcttcc tccgctacat ctccgactgg gacctagacc ctggcccgctg 300  
 ctaccgctgc acctgggttca cctcctggag ccctcgctac gactgtgccc gacatgtggc 360  
 cgactcttctg cgagggaacc ccaacctcag tctgaggatc ttcaccgcgc gctctactt 420  
 ctgtgaggac cgcaaggctg agcccgaggg gctgcggcgg ctgcaccgcg ccgggggtgca 480  
 aatagccatc atgaccttca aagattattt ttaactgtgg aatacttttg tagaaaacca 540  
 tgaagaacct ttcaaaagcct ggggaagggt gcatgaaaat tcaagtctgc tctccagaca 600  
 gcttogggoc atccttttgc cccctgtatga ggttgatgac ttaccgagac catttcgtac 660  
 ttgtggactt tgatagcaac ttccagggaat gtcacacacg atgaaatabc tctgctgaag 720  
 acagtggata aaaaacagtc ctccaagtct tctcgtttt tattcttcaa ctctcaactt 780  
 cttagagttt acagaaaaaa tatttatata cgactcttta aaaagatcta tgccttgaaa 840  
 atagagaagg aacacaggctc tggccaggga cgtgctgcaa ttggtgcagt ttgtaatgca 900  
 acattgtccc ctactgggaa taacagaact gcaggacctg ggagcatcct aaagtgtcaa 960  
 cgtttttcta tgaacttttag gtaggatgag agcagaagggt agatcctaaa aagcatgggt 1020  
 agaggatcaa atgttttttat atcaaatcct ttattattt gattcatttg agttaacagt 1080  
 ggtgttagtg atagattttt ctattctttt cccttgacgt ttaacttcaa gtaacacaaa 1140  
 ctcttcacat agggcatgat ctataggacc tctaataag agtatctggg tgattgtgac 1200  
 cccaaacatc cctccaaaag catataatc caatcatgcy ctgtatgttt taatcagcag 1260  
 aagcatgttt ttatgtttgt acaaaaagag attgttatgg gtggggatgg aggtatagac 1320  
 ctgcgatggt caacctcaag ctactttaat aaaggatcct aaaaatggca ggaggactgt 1380  
 gaacaaagca cccataaat ggggtgatgt ctgaagtatc aaatcttctg gaaacgcgaa 1440  
 ctcttttaag gaagtcctca atttagaacc acccacaac ttcacatc ataattagca 1500  
 aacaattgga aggaagtgtc ttgaatgttg gggagaggaa aatctattgg ctctcgtggg 1560  
 tctcttcac tcagaaatgc caatcaggtc aaggtttgct acattttgta tgbtgbtgbt 1620

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gcttctccca aaggtatatt aactatataa gagagttgtg acaaaacaga atgataaagc 1680
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cttgaacaca ggtgttccaag gccagcctgtg gcaacataac aagatcctgt cctctcaaaa 1800
aaaaaaaaaa aaaaagaaaag agagagggcc gggcggtggg gctcacgcct gtaatcccgag 1860
cactttggga ggccgagccg ggcggatcac ctgtggtcag gagtttgaga ccagcctggc 1920
caacatggca aaaccccgtc tgtactcaaa atgcaaaaat tagccaggcg tggtagcagg 1980
cacctgtaat cccagctact tgggaggctg aggcaggaga atcgcttgaa cccaggagg 2040
ggaggttgca gtaagctgag atcggtgccgt tgcactccag cctggggcagc aagagcaaga 2100
ctctgtctca gaaaaaaaaa aaaaaaagag agagagagag aaagagaca atatttggga 2160
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aatagggat cctatttggc ctcttttggc gtctatttgg cctaacaac tgcctttgac 2280
agtgaagaaa atattcagaa taaccatata cctgtgccgt tattacctag caacccctgc 2340
aatgaagatg agcagatoca caggaaaaact tgaatgcaca actgtcttat ttaaatctta 2400
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tattattttt cgtctaatga ttttttatta acatgatttc cttttctgat atattgaaat 2520
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atgacagcaa atttgcttct ggctcacttt caatcagtta aataaatgat aaataatttt 2700
ggaagctgtg aagataaaat accaaataaa ataataataa agtgatttat atgaagttaa 2760
aataaaaaat cagtatgatg gaataaactt g

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&lt;210&gt; 206

&lt;211&gt; 416

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 206

```

Pro Asn Ser Asn His Val Ala Ser Gly Ala Gly Glu Ala Ala Ile Glu
1 5 10 15

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Thr Gln Ser Ser Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro
20 25 30

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Pro Pro Leu Pro Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys
35 40 45

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```

Ser Ser Gly Tyr His Tyr Gly Val Ser Ala Cys Glu Gly Cys Lys Gly
50 55 60

```

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Phe Phe Arg Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg
65 70 75 80

```

```

Asp Lys Asn Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr
85 90 95

```

```

Cys Arg Leu Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ser Val
100 105 110

```

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Arg Asn Asp Arg Asn Lys Lys Lys Lys Glu Val Pro Lys Pro Glu Cys
115 120 125

```

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Ser Glu Ser Tyr Thr Leu Thr Pro Glu Val Gly Glu Leu Ile Glu Lys
130 135 140

```

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Val Arg Lys Ala His Gln Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly
145 150 155 160

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Lys Tyr Thr Thr Asn Asn Ser Ser Glu Gln Arg Val Ser Leu Asp Ile  
 165 170 175  
 Asp Leu Trp Asp Lys Phe Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys  
 180 185 190  
 Thr Val Glu Phe Ala Lys Gln Leu Pro Gly Phe Thr Thr Leu Thr Ile  
 195 200 205  
 Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys Leu Asp Ile Leu Ile  
 210 215 220  
 Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln Asp Thr Met Thr Phe  
 225 230 235 240  
 Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met His Asn Ala Gly Phe  
 245 250 255  
 Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala Asn Gln Leu Leu Pro  
 260 265 270  
 Leu Glu Met Asp Asp Ala Glu Thr Gly Leu Leu Ser Ala Ile Cys Leu  
 275 280 285  
 Ile Cys Gly Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met  
 290 295 300  
 Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Val Tyr Val Arg Lys Arg  
 305 310 315 320  
 Arg Pro Ser Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr  
 325 330 335  
 Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu  
 340 345 350  
 Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu  
 355 360 365  
 Glu Asn Ser Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly  
 370 375 380  
 Gly Arg Asp Gly Gly Gly Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro  
 385 390 395 400  
 Ser Leu Ser Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro  
 405 410 415

&lt;210&gt; 207

&lt;211&gt; 1284

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 207

cccaacagca accacgtggc cagtggcgcc ggggaggcag ccattgagac ccagagcagc 60  
 agttctgaag agatagtgcc cagccctccc tcgccacccc ctctaccocg catctacaag 120  
 ccttgctttg tctgtcagga caagtctcca ggcctaccact atgggggtcag cgcctgtgag 180

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```

ggctgcaagg gcttcttccg ccgcagcatc cagaagaaca tgggtgtcac gtgtcaccgg 240
gacaagaact gcatcatcaa caaggtgacc cgaacccgct gccagttact cgcactgcag 300
aagtgtcttg aagtgggcat gtccaaggag tctgtgagaa acgaccgaaa caagaagaag 360
aaggagggtgc ccaagcccca gtgctctgag agctacacgc tgacgcgcga ggtgggggag 420
ctcatgtgaga aggtgcgcaa agcgcaccag gaaaccttcc ctgccctctg ccagctgggc 480
aaatacacta cgaacaacag ctcaagaaca cgtgtctctc tggacattga cctctgggac 540
aagtctcagtg aactctccac caagtgcac attaaagctg tggagtctgc caagcagctg 600
cccggtctca ccacctccac catcgccgac cagatcaccc tctctcaaggc tgcctgcctg 660
gacatctgga tcttcgggat ctgcacggcg tacacgcccc agcaggacac catgaccttc 720
tcggaacgggc tgacctcgaa ccggaaccag atgcacaacg ctggcttcgg cccctcacc 780
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cgggtggaca tcttcgagga gccgtctctg gaggcgctaa aggtctactg cgggaagcgg 960
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agcctcagcc ccagctccaa cagaagcagc ccggccacc actcccgctg accgccacg 1260
ccacatggac acagccctcg cctt 1284

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&lt;210&gt; 208

&lt;211&gt; 797

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 208

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Met Glu Pro Ala Pro Ala Arg Ser Pro Arg Pro Gln Gln Asp Pro Ala
  1           5           10          15

Arg Pro Gln Glu Pro Thr Met Pro Pro Pro Glu Thr Pro Ser Glu Gly
  20           25           30

Arg Gln Pro Ser Pro Ser Pro Ser Pro Thr Glu Arg Ala Pro Ala Ser
  35           40           45

Glu Glu Glu Phe Gln Phe Leu Arg Cys Gln Gln Cys Gln Ala Glu Ala
  50           55           60

Lys Cys Pro Lys Leu Leu Pro Cys Leu His Thr Leu Cys Ser Gly Cys
  65           70           75           80

Leu Glu Ala Ser Gly Met Gln Cys Pro Ile Cys Gln Ala Pro Trp Pro
  85           90           95

Leu Glu Ala Asp Thr Pro Ala Leu Asp Asn Val Phe Phe Glu Ser Leu
 100          105          110

Gln Arg Arg Leu Ser Val Tyr Arg Gln Ile Val Asp Ala Gln Ala Val
 115          120          125

Cys Thr Arg Cys Lys Glu Ser Ala Asp Phe Trp Cys Phe Glu Cys Glu
 130          135          140

Gln Leu Leu Cys Ala Lys Cys Phe Glu Ala His Gln Trp Phe Leu Lys
 145          150          155          160

His Glu Ala Arg Pro Leu Ala Glu Leu Arg Asn Gln Ser Val Arg Glu

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165	170	175
Phe Leu Asp Gly Thr Arg Lys Thr Asn Asn Ile Phe Cys Ser Asn Pro		
180	185	190
Asn His Arg Thr Pro Thr Leu Thr Ser Ile Tyr Cys Arg Gly Cys Ser		
195	200	205
Lys Pro Leu Cys Cys Ser Cys Ala Leu Leu Asp Ser Ser His Ser Glu		
210	215	220
Leu Lys Cys Asp Ile Ser Ala Glu Ile Gln Gln Arg Gln Glu Glu Leu		
225	230	235
Asp Ala Met Thr Gln Ala Leu Gln Glu Gln Asp Ser Ala Phe Gly Ala		
245	250	255
Val His Ala Gln Met His Ala Ala Val Gly Gln Leu Gly Arg Ala Arg		
260	265	270
Ala Glu Thr Glu Glu Leu Ile Arg Glu Arg Val Arg Gln Val Val Ala		
275	280	285
His Val Arg Ala Gln Glu Arg Glu Leu Leu Glu Ala Val Asp Ala Arg		
290	295	300
Tyr Gln Arg Asp Tyr Glu Glu Met Ala Ser Arg Leu Gly Arg Leu Asp		
305	310	315
Ala Val Leu Gln Arg Ile Arg Thr Gly Ser Ala Leu Val Gln Arg Met		
325	330	335
Lys Cys Tyr Ala Ser Asp Gln Glu Val Leu Asp Met His Gly Phe Leu		
340	345	350
Arg Gln Ala Leu Cys Arg Leu Arg Gln Glu Glu Pro Gln Ser Leu Gln		
355	360	365
Ala Ala Val Arg Thr Asp Gly Phe Asp Glu Phe Lys Val Arg Leu Gln		
370	375	380
Asp Leu Ser Ser Cys Ile Thr Gln Gly Lys Ala Ile Glu Thr Gln Ser		
385	390	395
Ser Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro Pro Pro Leu		
405	410	415
Pro Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys Ser Ser Gly		
420	425	430
Tyr His Tyr Gly Val Ser Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg		
435	440	445
Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg Asp Lys Asn		
450	455	460
Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr Cys Arg Leu		
465	470	475
		480

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Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ser Val Arg Asn Asp  
 485 490 495  
 Arg Asn Lys Lys Lys Lys Glu Val Pro Lys Pro Glu Cys Ser Glu Ser  
 500 505 510  
 Tyr Thr Leu Thr Thr Pro Glu Val Gly Glu Leu Ile Glu Lys Val Arg Lys  
 515 520 525  
 Ala His Gln Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly Lys Tyr Thr  
 530 535 540  
 Thr Asn Asn Ser Ser Glu Gln Arg Val Ser Leu Asp Ile Asp Leu Trp  
 545 550 555 560  
 Asp Lys Phe Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys Thr Val Glu  
 565 570 575  
 Phe Ala Lys Gln Leu Pro Gly Phe Thr Thr Leu Thr Ile Ala Asp Gln  
 580 585 590  
 Ile Thr Leu Leu Lys Ala Ala Cys Leu Asp Ile Leu Ile Leu Arg Ile  
 595 600 605  
 Cys Thr Arg Tyr Thr Thr Pro Glu Gln Asp Thr Met Thr Phe Ser Asp Gly  
 610 615 620  
 Leu Thr Leu Asn Arg Thr Gln Met His Asn Ala Gly Phe Gly Pro Leu  
 625 630 635 640  
 Thr Asp Leu Val Phe Ala Phe Ala Asn Gln Leu Leu Pro Leu Glu Met  
 645 650 655  
 Asp Asp Ala Glu Thr Gly Leu Leu Ser Ala Ile Cys Leu Ile Cys Gly  
 660 665 670  
 Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met Leu Gln Glu  
 675 680 685  
 Pro Leu Leu Glu Ala Leu Lys Val Tyr Val Arg Lys Arg Arg Pro Ser  
 690 695 700  
 Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr Asp Leu Arg  
 705 710 715 720  
 Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu Lys Met Glu  
 725 730 735  
 Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu Glu Asn Ser  
 740 745 750  
 Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly Gly Gly Arg Asp  
 755 760 765  
 Gly Gly Gly Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro Ser Leu Ser  
 770 775 780

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Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro  
785 790 795

<210> 209  
<211> 3036  
<212> DNA  
<213> Homo sapiens

<400> 209  
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caggagccca ccatgcctcc ccccgagacc cctctgaag gccgccagcc cagcccccagc 180  
cccagcccta cagagcgagc ccccgcttgc gaggaggagt tccagtttct cagctgcccag 240  
caatgccagg cggaaagcaa gtgcocgaag ctgctgcctt gtctgcacac gctgtgctca 300  
ggatgcctgg aggcgtcggg catgcagtcg ccatctgcc aggcgcctctg gcccttaggt 360  
cgagacacac ccgcctctgga taacgtcttt ttcgagatgc tgcagcggcg cctgtcgggt 420  
taccgcagga ttgtggatgc gcaggctgtg tgcaaccgct gcaaaagatg gcccgacttc 480  
tggtgctttg agtgcagcga gctcctctgc gccaaagtgt tgcaggcaca ccagtgttcc 540  
ctcaagcacg aggcgcggcc cctagcagag ctgcgcacac agtcgggtgc tgagtctcctg 600  
gacggcaccc gcaagaccaa caacatcttc tgcctcaacc ccaaccaccg caccctctacg 660  
ctgaccacga tctactgcgg aggatgttcc aagccgctgt gctgctctgt cgcgctcctt 720  
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&lt;210&gt; 210

&lt;211&gt; 99

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 210

Asp Val Ser Asn Thr Thr Thr Ala Gln Lys Arg Lys Cys Ser Gln Thr  
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Gln Cys Pro Arg Lys Val Ile Lys Met Glu Ser Glu Glu Gly Lys Glu  
 20 25 30

Ala Arg Leu Ala Leu Pro Ala Pro Gly Pro Tyr Ser Thr Pro Leu Arg  
 35 40 45

Thr Pro Leu Trp Asn Gly Ser Asn His Ser Ile Glu Thr Gln Ser Ser  
 50 55 60

Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro Pro Pro Leu Pro  
 65 70 75 80

Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys Ser Ser Gly Tyr  
 85 90 95

His Tyr Gly

&lt;210&gt; 211

&lt;211&gt; 296

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 211

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 ggtccgctact ccaccccgct ccggactccg ctttggaatg gctcaaaacca ctccattgag 180  
 acccagagca gcagttctga agagatagtg cccagccctc cctcgccacc cctctaccc 240  
 cgcattcaca agccttgctt tgtctgtcag gacaagtctc caggctacca ctatgg 296

&lt;210&gt; 212

&lt;211&gt; 673

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 212

Met Asp Leu Thr Lys Met Gly Met Ile Gln Leu Gln Asn Pro Ser His  
 1 5 10 15

Pro Thr Gly Leu Leu Cys Lys Ala Asn Gln Met Arg Leu Ala Gly Thr  
 20 25 30

Leu Cys Asp Val Val Ile Met Val Asp Ser Gln Glu Phe His Ala His

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35	40	45
Arg Thr Val Leu Ala Cys	Thr Ser Lys Met Phe Glu	Ile Leu Phe His
50	55	60
Arg Asn Ser Gln His Tyr	Thr Leu Asp Phe Leu Ser	Pro Lys Thr Phe
65	70	75
Gln Gln Ile Leu Glu Tyr	Ala Tyr Thr Ala Thr	Leu Gln Ala Lys Ala
85	90	95
Glu Asp Leu Asp Asp Leu	Leu Tyr Ala Ala Glu	Ile Leu Glu Ile Glu
100	105	110
Tyr Leu Glu Glu Gln Cys	Leu Lys Met Leu Glu	Thr Ile Gln Ala Ser
115	120	125
Asp Asp Asn Asp Thr Glu	Ala Thr Met Ala Asp	Gly Gly Ala Glu Glu
130	135	140
Glu Glu Asp Arg Lys Ala	Arg Tyr Leu Lys Asn	Ile Phe Ile Ser Lys
145	150	155
His Ser Ser Glu Glu Ser	Gly Tyr Ala Ser Val	Ala Gly Gln Ser Leu
165	170	175
Pro Gly Pro Met Val Asp	Gln Ser Pro Ser Val	Ser Thr Ser Phe Gly
180	185	190
Leu Ser Ala Met Ser Pro	Thr Lys Ala Ala Val	Asp Ser Leu Met Thr
195	200	205
Ile Gly Gln Ser Leu Leu	Gln Gly Thr Leu Gln	Pro Pro Ala Gly Pro
210	215	220
Glu Glu Pro Thr Leu Ala	Gly Gly Gly Arg His	Pro Gly Val Ala Glu
225	230	235
Val Lys Thr Glu Met Met	Gln Val Asp Glu Val	Pro Ser Gln Asp Ser
245	250	255
Pro Gly Ala Ala Glu Ser	Ser Ile Ser Gly Gly	Met Gly Asp Lys Val
260	265	270
Glu Glu Arg Gly Lys Glu	Gly Pro Gly Thr Pro	Thr Arg Ser Ser Val
275	280	285
Ile Thr Ser Ala Arg Glu	Leu His Tyr Gly Arg	Glu Glu Ser Ala Glu
290	295	300
Gln Val Pro Pro Pro Ala	Glu Ala Gly Gln Ala	Pro Thr Gly Arg Pro
305	310	315
Glu His Pro Ala Pro Pro	Pro Glu Lys His Leu	Gly Ile Tyr Ser Val
325	330	335
Leu Pro Asn His Lys Ala	Asp Ala Val Leu Ser	Met Pro Ser Ser Val
340	345	350

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Thr Ser Gly Leu His Val Gln Pro Ala Leu Ala Val Ser Met Asp Phe  
 355 360 365  
 Ser Thr Tyr Gly Gly Leu Leu Pro Gln Gly Phe Ile Gln Arg Glu Leu  
 370 375 380  
 Phe Ser Lys Leu Gly Glu Leu Ala Val Gly Met Lys Ser Glu Ser Arg  
 385 390 395 400  
 Thr Ile Gly Glu Gln Cys Ser Val Cys Gly Val Glu Leu Pro Asp Asn  
 405 410 415  
 Glu Ala Val Glu Gln His Arg Lys Leu His Ser Gly Met Lys Thr Tyr  
 420 425 430  
 Gly Cys Glu Leu Cys Gly Lys Arg Phe Leu Asp Ser Leu Arg Leu Arg  
 435 440 445  
 Met His Leu Leu Ala His Ser Ala Gly Ala Lys Ala Phe Val Cys Asp  
 450 455 460  
 Gln Cys Gly Ala Gln Phe Ser Lys Glu Asp Ala Leu Glu Thr His Arg  
 465 470 475 480  
 Gln Thr His Thr Gly Thr Asp Met Ala Val Phe Cys Leu Leu Cys Gly  
 485 490 495  
 Lys Arg Phe Gln Ala Gln Ser Ala Leu Gln Gln His Met Glu Val His  
 500 505 510  
 Ala Gly Val Arg Ser Tyr Ile Cys Ser Glu Cys Asn Arg Thr Phe Pro  
 515 520 525  
 Ser His Thr Ala Leu Lys Arg His Leu Arg Ser His Thr Gly Asp His  
 530 535 540  
 Pro Tyr Glu Cys Glu Phe Cys Gly Ser Cys Phe Arg Asp Glu Ser Thr  
 545 550 555 560  
 Leu Lys Ser His Lys Arg Ile His Thr Gly Glu Lys Pro Tyr Glu Cys  
 565 570 575  
 Asn Gly Cys Asp Lys Lys Phe Ser Leu Lys His Gln Leu Glu Thr His  
 580 585 590  
 Tyr Arg Val His Thr Gly Glu Lys Pro Phe Glu Cys Lys Leu Cys His  
 595 600 605  
 Gln Arg Ser Arg Asp Tyr Ser Ala Met Ile Lys His Leu Arg Thr His  
 610 615 620  
 Asn Gly Ala Ser Pro Tyr Gln Cys Thr Ile Cys Thr Glu Tyr Cys Pro  
 625 630 635 640  
 Ser Leu Ser Ser Met Gln Lys His Met Lys Gly His Lys Pro Glu Glu  
 645 650 655

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Ile Pro Pro Asp Trp Arg Ile Glu Lys Thr Tyr Leu Tyr Leu Cys Tyr  
 660 665 670

Val.

<210> 213  
 <211> 2197  
 <212> DNA  
 <213> Homo sapiens

<400> 213  
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 caccocacgg ggctactgtg caaggccaac cagatgcggc tggccgggac ttgtgctgat 180  
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 gccggaggacc tggatgacct gctgtatgcg gccagatccc tggagatcga gtacctggag 420  
 gaacagtgcc tgaagatgct ggagaccatc caggcctcag acgacaatga caggaggccc 480  
 accatggccg atggcggggc caggaagaaa gaggaccgca aggctcggta cctcaagaac 540  
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 acagagtact gccccagcct ctctctccat cagaagcaca tgaagggcca caagcccgag 2040  
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 gaggcccgcc gccgttgagc cagacggggg gccaggaaaag aagagttgga gtgagatgaa 2160  
 ggaaggacta tgacaaataa aaaaaaaaaa ggaattc 2197

<210> 214  
 <211> 673  
 <212> PRT  
 <213> Homo sapiens

<400> 214  
 Met Asp Leu Thr Lys Met Gly Met Ile Gln Leu Gln Asn Pro Ser His

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1	5	10	15
Pro Thr Gly Leu Leu Cys Lys Ala Asn Gln Met Arg Leu Ala Gly Thr	20	25	30
Leu Cys Asp Val Val Ile Met Val Asp Ser Gln Glu Phe His Ala His	35	40	45
Arg Thr Val Leu Ala Cys Thr Ser Lys Met Phe Glu Ile Leu Phe His	50	55	60
Arg Asn Ser Gln His Tyr Thr Leu Asp Phe Leu Ser Pro Lys Thr Phe	65	70	75
Gln Gln Ile Leu Glu Tyr Ala Tyr Thr Ala Thr Leu Gln Ala Lys Ala	85	90	95
Glu Asp Leu Asp Asp Leu Leu Tyr Ala Ala Glu Ile Leu Glu Ile Glu	100	105	110
Tyr Leu Glu Glu Gln Cys Leu Lys Met Leu Glu Thr Ile Gln Ala Ser	115	120	125
Asp Asp Asn Asp Thr Glu Ala Thr Met Ala Asp Gly Gly Ala Glu Glu	130	135	140
Glu Glu Asp Arg Lys Ala Arg Tyr Leu Lys Asn Ile Phe Ile Ser Lys	145	150	155
His Ser Ser Glu Glu Ser Gly Tyr Ala Ser Val Ala Gly Gln Ser Leu	165	170	175
Pro Gly Pro Met Val Asp Gln Ser Pro Ser Val Ser Thr Ser Phe Gly	180	185	190
Leu Ser Ala Met Ser Pro Thr Lys Ala Ala Val Asp Ser Leu Met Thr	195	200	205
Ile Gly Gln Ser Leu Leu Gln Gly Thr Leu Gln Pro Pro Ala Gly Pro	210	215	220
Glu Glu Pro Thr Leu Ala Gly Gly Gly Arg His Pro Gly Val Ala Glu	225	230	235
Val Lys Thr Glu Met Met Gln Val Asp Glu Val Pro Ser Gln Asp Ser	245	250	255
Pro Gly Ala Ala Glu Ser Ser Ile Ser Gly Gly Met Gly Asp Lys Val	260	265	270
Glu Glu Arg Gly Lys Glu Gly Pro Gly Thr Pro Thr Arg Ser Ser Val	275	280	285
Ile Thr Ser Ala Arg Glu Leu His Tyr Gly Arg Glu Glu Ser Ala Glu	290	295	300
Gln Val Pro Pro Pro Ala Glu Ala Gly Gln Ala Pro Thr Gly Arg Pro	305	310	315
			320



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Glu His Pro Ala Pro Pro Pro Glu Lys His Leu Gly Ile Tyr Ser Val  
 325 330 335  
 Leu Pro Asn His Lys Ala Asp Ala Val Leu Ser Met Pro Ser Ser Val  
 340 345 350  
 Thr Ser Gly Leu His Val Gln Pro Ala Leu Ala Val Ser Met Asp Phe  
 355 360 365  
 Ser Thr Tyr Gly Gly Leu Leu Pro Gln Gly Phe Ile Gln Arg Glu Leu  
 370 375 380  
 Phe Ser Lys Leu Gly Glu Leu Ala Val Gly Met Lys Ser Glu Ser Arg  
 385 390 395 400  
 Thr Ile Gly Glu Gln Cys Ser Val Cys Gly Val Glu Leu Pro Asp Asn  
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 Glu Ala Val Glu Gln His Arg Lys Leu His Ser Gly Met Lys Thr Tyr  
 420 425 430  
 Gly Cys Glu Leu Cys Gly Lys Arg Phe Leu Asp Ser Leu Arg Leu Arg  
 435 440 445  
 Met His Leu Leu Ala His Ser Ala Gly Ala Lys Ala Phe Val Cys Asp  
 450 455 460  
 Gln Cys Gly Ala Gln Phe Ser Lys Glu Asp Ala Leu Glu Thr His Arg  
 465 470 475 480  
 Gln Thr His Thr Gly Thr Asp Met Ala Val Phe Cys Leu Leu Cys Gly  
 485 490 495  
 Lys Arg Phe Gln Ala Gln Ser Ala Leu Gln Gln His Met Glu Val His  
 500 505 510  
 Ala Gly Val Arg Ser Tyr Ile Cys Ser Glu Cys Asn Arg Thr Phe Pro  
 515 520 525  
 Ser His Thr Ala Leu Lys Arg His Leu Arg Ser His Thr Gly Asp His  
 530 535 540  
 Pro Tyr Glu Cys Glu Phe Cys Gly Ser Cys Phe Arg Asp Glu Ser Thr  
 545 550 555 560  
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 565 570 575  
 Asn Gly Cys Asp Lys Lys Phe Ser Leu Lys His Gln Leu Glu Thr His  
 580 585 590  
 Tyr Arg Val His Thr Gly Glu Lys Pro Phe Glu Cys Lys Leu Cys His  
 595 600 605  
 Gln Arg Ser Arg Asp Tyr Ser Ala Met Ile Lys His Leu Arg Thr His  
 610 615 620

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Asn Gly Ala Ser Pro Tyr Gln Cys Thr Ile Cys Thr Glu Tyr Cys Pro  
625 630 635 640

Ser Leu Ser Ser Met Gln Lys His Met Lys Gly His Lys Pro Glu Glu  
645 650 655

Ile Pro Pro Asp Trp Arg Ile Glu Lys Thr Tyr Leu Tyr Leu Cys Tyr  
660 665 670

Val

&lt;210&gt; 215

&lt;211&gt; 2197

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 215

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tgcaatggct ttgacaagaa gttcagcctc aagcatcagc ttgagacgca ctatagggtg 1860
cacacaggtg agaagccctt tgagtgtaa cctctgccac agcgctcccg ggaactactg 1920
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acagagtact gcccccagct ctctccatg cagaagcaca tgaagggcca cagcccgag 2040
gagatcccgc ccgactggag gatagagaag acgtacctct acctgtgcta tgtgtgaag 2100
gaggcccgcg gcggtggagc cgagcgggga gccaggaaag aagagtggga gtgagatgaa 2160
ggaaggacta tgacaaataa aaaaaaaaaa ggaattc 2197

```

&lt;210&gt; 216

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&lt;211&gt; 29

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 216

Arg Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Glu  
1 5 10 15

Leu Leu Gln Glu Glu Thr Arg Gln Lys Leu Asn Val Ser  
20 25

&lt;210&gt; 217

&lt;211&gt; 89

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 217

acgcgaattt gaagatagag acaggtctca tcgggaggaa atggaggagc tgcttcaaga 60  
agaaaccccg cagaagctca acgtgtcta 89

&lt;210&gt; 218

&lt;211&gt; 26

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 218

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Phe Lys  
1 5 10 15

Arg Ala Lys Ala Asn Leu Asp Lys Asn Lys  
20 25

&lt;210&gt; 219

&lt;211&gt; 78

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 219

gaatttgaag atagagacag gtctcatcgg gaggaatagg agttcaagag ggccaaggcg 60  
aacctagaca agaataag 78

&lt;210&gt; 220

&lt;211&gt; 34

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 220

Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Val His  
1 5 10 15

Glu Leu Glu Lys Ser Lys Arg Ala Leu Glu Thr Gln Met Glu Glu Met  
20 25 30

Lys Thr

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<210> 221  
<211> 102  
<212> DNA  
<213> Homo sapiens

<400> 221  
gaatttgaag atagagacag gtctcatcgg gaggaatgg aggtccatga gctggagaag 60  
tccaagcggg ccctggagac ccagatggag gagatgaaga cg 102

<210> 222  
<211> 50  
<212> PRT  
<213> Homo sapiens

<400> 222  
Glu Phe Glu Asp Arg Asp Arg Ser His Arg Glu Glu Met Glu Asn Glu  
1 5 10 15  
Val Glu Ser Val Thr Gly Met Leu Asn Glu Ala Glu Gly Lys Ala Ile  
20 25 30  
Lys Leu Ala Lys Asp Val Ala Ser Leu Ser Ser Gln Leu Gln Asp Thr  
35 40 45  
Gln Glu  
50

<210> 223  
<211> 152  
<212> DNA  
<213> Homo sapiens

<400> 223  
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acagggatgc ttaacgaggc cgaggggaag gccattaagc tggccaagga cgtggcgtcc 120  
ctcagttccc agctccagga caccacaggag tt 152

<210> 224  
<211> 1353  
<212> DNA  
<213> Homo sapiens

<220>  
<221> modified\_base  
<222> (941)  
<223> a, c, t, g, other or unknown

<220>  
<221> modified\_base  
<222> (1067)  
<223> a, c, t, g, other or unknown

<220>

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<221> modified\_base  
 <222> (1077)  
 <223> a, c, t, g, other or unknown

<400> 224  
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 taccataagg ggtttaaata ggaatgtttt ctccaaagtg aatcttggaa tctttgggtt 180  
 tataattgtc aagcctcttt ttttaaaata gatttgggtc acaggaagta ttttttcta 240  
 attttatttt tatagacct gtcaagcttc ttaattgtta aatattgtta taacaataca 300  
 tctgggcccgg gcggcgttgc tcaactcgtt aatcccagca ctltggggagg ccaggggcgg 360  
 tgaatcacga ggtcaggaga ttgagaccat cctggctaac acaagaagaa cccatctcta 420  
 ctaaaaaac aaaaaattag ctggggaggagg agggggggcg cgttagtccc agctactcgg 480  
 gaggcggagc ttggcgttgc ccaagatcgc gccactgcac tccagcgact ccgtctcaaa 540  
 aaaaaaaaa aaaaacatc tgaagtgcga catggttgtt agccgaggag aaaaacatc 600  
 ctccaaata cgcggtatgag agggacagag ctgaggcaga agccaggagg aaggaacca 660  
 aggcctctgc cctggctcgg gcccttgaag aggccttga agccaaagag gaactcgagc 720  
 ggaccaaaca aatgctcaaa gccgaatgg aagacctggt cagctccaa gatgaactgg 780  
 cgaagaacgt aagtgcctct ggggtgtttt tctcgtccat gtttcgctcg cccaacctct 840  
 gtgctattca ccagtcctat cgaggctagc tcttggcctt tttcatagcg aactatcatc 900  
 ggaatgtgaa ggaggttttt ggaactgtgc aggggctaaa naggggctga gaatggcagt 960  
 cgaggatggg totgagtgg ggggtccgag gataaggctg gggctctgaac tctcaggggt 1020  
 catcttgagt cccggccatg catcctgtgg gaggccaaag ccacctnccc tgatctnccc 1080  
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 cagatggagg agatgaagac gcagctggaa gagctggagg acgagctgca agccacggag 1260  
 gacgcacaa tcgggctgga agtcaacatg caggcgctca agggccagtt cgaaaaggat 1320  
 ctccaagccc gggacgagca gaatgaggag aag 1353

<210> 225  
 <211> 744  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> modified\_base  
 <222> (326)  
 <223> a, c, t, g, other or unknown

<220>  
 <221> modified\_base  
 <222> (614)  
 <223> a, c, t, g, other or unknown

<400> 225  
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 taatctaagt ggtctgtagc agctgaggat gtccccaaga atacttggta gctaagagaa 120  
 gaaaatggag ggaatatatg gataacttgt ttctttgatg ctgttgtaat tcttgtatt 180  
 ttcatatatg tgaatacaag acttccacac catgcccctt ctcttcggtat ctgtaaaatt 240  
 tagaagcttt aaaaagtata ttgtacattt gttacatttc tgaacctttt tgctcatgct 300  
 ctttgttccc tgatgtagaa tgttcnattc tgtcogtcaa ggcccaacct gaatgttgtc 360  
 attaaatgct aggcctttcc tcagtctctg gggctctgaac tgctcagggg tcatcttgag 420  
 tccggccatc gcatcctgtg ggaggccaaa gccacctccc tgatctctg aggtgcgcgt 480  
 caggtgtggg ttctcaatcg tcttcatgaa gttgagcctc atagaatggg gctgcccgct 540  
 ctgcggcgag tcccatgagc tggagaagtc caagcgggccc ctggagaccg agatggagga 600  
 gatgaagacg cagntggaag agctggagga cgagctgcaa gccacggagg acgccaaact 660  
 gcggctggaa gtcaacatgc aggcgtcaa gggccagttc gaaaggagtc tccaagcccg 720

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ggacgagcag aatgaggaga agag

744

&lt;210&gt; 226

&lt;211&gt; 60

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 226

tctctgtgcc agtagtgggc atgtagagga ccctaataagg agtattcata ccagcagcag 60

&lt;210&gt; 227

&lt;211&gt; 25

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 227

Met Pro Arg Phe Gly Phe Gln Ile Gly Val Arg Tyr Glu Asn Lys Lys  
1 5 10 15Arg Glu Asn Leu Ala Leu Thr Leu Leu  
20 25

&lt;210&gt; 228

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 228

agctctcctt) gcagcccgag ctgaccctag gcctccaccc tggcaggaat cccaatttgc 60  
ctccacttag tgagcggaag aatgtgctac agttgaaact ccagcagcgc cggaccgggg 120  
aagaactggt gagccaaggg atcatgccgc ggtttggttt tcagatagga gttaggtatg 180  
agaacaagaa gagagaaaac ttggcgctga ccctgttata gtggttatag tgggtgcctt 240  
aaaggaggga aatgatttca gcaaaactgg ttgaacagcg gatgaagata tgggaattcaa 300

&lt;210&gt; 229

&lt;211&gt; 43

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 229

Lys Met Arg Lys Met Glu Asp Asn Gln Tyr Ser Glu Ala Glu Leu Ser  
1 5 10 15Ser Phe Ser Thr Ser His Val Pro Glu Glu Leu Lys Gln Pro Leu His  
20 25 30Arg Lys Ser Lys Ser Gln Val Gln Ile Phe Pro  
35 40

&lt;210&gt; 230

&lt;211&gt; 916

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

```

<400> 230
aaaatgagga aaatggaaga taatcaatat tctgaagctg agctgtcttc ttttagtact 60
tccccatggc cagaggaact taagcagcgc ttacacagaa agtccaaatc gcagggtacag 120
attttcccat agtacagcat catgggttaca ttatgcatga aacgtacatt tcctttgatt 180
accaaaaagc aaatatctcta tctttgaaat attttagaat ccaaatgggg tcagatgcct 240
ttctaaaaat gttcatactct ttactgtatt tatgaccaa tccaaaaatag ttaagcaaga 300
aagcaattaa tttagctgca ttctgtatag aaattttatg acaagcccca tctcacactt 360
atctttcctt gactttgcaa ttctcttact ttgtacagt tagttcatca tgtttgttta 420
caaatattta tgtattacct cagagtcatt ttccgtgtct atactttttg tcaatgtaat 480
tatattttaa gattttctg aaaagtgaat tctatttttt gtccctcttc atgtctagta 540
aattgttagg tgtagttaat tagcaagtc tctcatgttg caatttaata gtcaaatgag 600
gatcagcaag gaagtgaatt gccaaaggtc tacaccaact tactggcaga ttgggaaata 660
aaacctgtca atttaaattc aacaaatgaa tgagtgaatg aatggtactc aaatttatta 720
ggctctacaa cattgtatca gcactatggt aactaaaaat aaatctattt aagggtccat 780
aaatagcaat taaaagacc tcagtgtttt tgttacaaaa taaaggaagt cggtactttt 840
ttgtttgaca tccacactca accggattgt tcattcaggt caatataaaa taaagaaact 900
tcctattacc aaaaaa
916

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<210> 231
<211> 268
<212> PRT
<213> Homo sapiens

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```

<400> 231
Met Phe Arg Met Leu Asn Ser Ser Phe Glu Asp Asp Pro Phe Phe Ser
1 5 10 15

Glu Ser Ile Leu Ala His Arg Glu Asn Met Arg Gln Met Ile Arg Ser
20 25 30

Phe Ser Glu Pro Phe Gly Arg Asp Leu Leu Ser Ile Ser Asp Gly Arg
35 40 45

Gly Arg Ala His Asn Arg Arg Gly His Asn Asp Gly Glu Asp Ser Leu
50 55 60

Thr His Thr Asp Val Ser Ser Phe Gln Thr Met Asp Gln Met Val Ser
65 70 75 80

Asn Met Arg Asn Tyr Met Gln Lys Leu Glu Arg Asn Phe Gly Gln Leu
85 90 95

Ser Val Asp Pro Asn Gly His Ser Phe Cys Ser Ser Ser Val Met Thr
100 105 110

Tyr Ser Lys Ile Gly Asp Glu Pro Pro Lys Val Phe Gln Ala Ser Thr
115 120 125

Gln Thr Arg Arg Ala Pro Gly Gly Ile Lys Glu Thr Arg Lys Ala Met
130 135 140

Arg Asp Ser Asp Ser Gly Leu Glu Lys Met Ala Ile Gly His His Ile
145 150 155 160

His Asp Arg Ala His Val Ile Lys Lys Ser Lys Asn Lys Lys Thr Gly
165 170 175

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Asp Glu Glu Val Asn Gln Glu Phe Ile Asn Met Asn Glu Ser Asp Ala  
180 185 190

His Ala Phe Asp Glu Glu Trp Gln Ser Glu Val Leu Lys Tyr Lys Pro  
195 200 205

Gly Arg His Asn Leu Gly Asn Thr Arg Met Arg Ser Val Gly His Glu  
210 215 220

Asn Pro Gly Ser Arg Glu Leu Lys Arg Arg Glu Lys Pro Gln Gln Ser  
225 230 235 240

Pro Ala Ile Glu His Gly Arg Arg Ser Asn Val Leu Gly Asp Lys Leu  
245 250 255

His Ile Lys Gly Ser Ser Val Lys Ser Asn Lys Lys  
260 265

&lt;210&gt; 232

&lt;211&gt; 1116

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 232

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gttatgtgtt cccgtccgta ctggaggcta gctctgtctg cggccgcggc gagttaacat 60
cgtttttcca atctgtccgc ggctgccgcc acccaagaca gagccagaat gttcaggatg 120
ctgaacagca gttttgagga tgaccctctc ttctctgagt ccattctctg acaccggagaa 180
aatatgcgac agatgataag aagtttttct gaaccctttg gaagagacct gctcagatc 240
tctgatggta gagggagagc tcataatcgt agaggacata atgatggta agattctttg 300
actcatcacg atgtcagctc ttccagacc atggaccaaa tgggtgtcaaa tatgagaaac 360
tatatgcaga aattagaaga aaacttcgtt caactttcag tggatccaaa tggacattca 420
ttttgttctt cctcagttat gacttattcc aaaataggag atgaaccgcc aaaggttttt 480
caggcctcaa ctcaaatctg tcgagctcca ggaggaataa aggaaccagc gaaagcaatg 540
agagattctg acagtggact agaaaaaatg gctattggtc atcatatcca tgaccgagct 600
catgtcatta aaaagtcaaa gaacaagaag actggagatg aagagggtcaa ccaggagtgc 660
atcaatatga atgaagcga tgctcatgct ttgatgagg agtggcaaa gagggttttg 720
aagtacaac caggacgaca caacttagga aacactagaa tgagaagtgt tggccatgag 780
aatcctggct ccgcagaact taaaagaagg gagaaacctc aacaaagtcc agccattgaa 840
catggaaagg gatcaaatgt ttggggggac aaactccaca tcaagggtc atctgtgaaa 900
agcaacaaaa aataaatagc catgcatttg atttgttag ttttgattgt ttaaacagtt 960
agtaatgggt ctgggtata agcataagac caatctcttg ctgttaaatc agtctctgct 1020
ttggcaactt tctctgata tctgaatgtt catgaaggtc ctagctttat attgtccctc 1080
ttttaggaat aaaattttga ttttcaacaa aaaaaa 1116

```

&lt;210&gt; 233

&lt;211&gt; 268

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 233

Met Phe Arg Met Leu Asn Ser Ser Phe Glu Asp Asp Pro Phe Phe Ser  
1 5 10 15

Glu Ser Ile Leu Ala His Arg Glu Asn Met Arg Gln Met Ile Arg Ser  
20 25 30



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Phe Ser Glu Pro Phe Gly Arg Asp Leu Leu Ser Ile Ser Asp Gly Arg  
 35 40 45  
 Gly Arg Ala His Asn Arg Arg Gly His Asn Asp Gly Glu Asp Ser Leu  
 50 55 60  
 Thr His Thr Asp Val Ser Ser Phe Gln Thr Met Asp Gln Met Val Ser  
 65 70 75 80  
 Asn Met Arg Asn Tyr Met Gln Lys Leu Glu Arg Asn Phe Gly Gln Leu  
 85 90 95  
 Ser Val Asp Pro Asn Gly His Ser Phe Cys Ser Ser Ser Val Met Thr  
 100 105 110  
 Tyr Ser Lys Ile Gly Asp Glu Pro Pro Lys Val Phe Gln Ala Ser Thr  
 115 120 125  
 Gln Thr Arg Arg Ala Pro Gly Gly Ile Lys Glu Thr Arg Lys Ala Met  
 130 135 140  
 Arg Asp Ser Asp Ser Gly Leu Glu Lys Met Ala Ile Gly His His Ile  
 145 150 155 160  
 His Asp Arg Ala His Val Ile Lys Lys Ser Lys Asn Lys Lys Thr Gly  
 165 170 175  
 Asp Glu Glu Val Asn Gln Glu Phe Ile Asn Met Asn Glu Ser Asp Ala  
 180 185 190  
 His Ala Phe Asp Glu Glu Trp Gln Ser Glu Val Leu Lys Tyr Lys Pro  
 195 200 205  
 Gly Arg His Asn Leu Gly Asn Thr Arg Met Arg Ser Val Gly His Glu  
 210 215 220  
 Asn Pro Gly Ser Arg Glu Leu Lys Arg Arg Glu Lys Pro Gln Gln Ser  
 225 230 235 240  
 Pro Ala Ile Glu His Gly Arg Arg Ser Asn Val Leu Gly Asp Lys Leu  
 245 250 255  
 His Ile Lys Gly Ser Ser Val Lys Ser Asn Lys Lys  
 260 265

&lt;210&gt; 234

&lt;211&gt; 1130

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 234

agtgaggcgt cgtccgtact ggaggctagc tcttgcgcgc gccgcggcga gttaacatcg 60  
 tttttccaat ctgtccgcgc ctgccaccac ccaagacaga gccagaatgt tcaggatgct 120  
 gaacagcagc tttgaggatg accccttctt ctctgagtcac attcttgcac acogagaaaa 180  
 tatgcgacag atgataagaa gttttttctga accctttgga agagacttgc tcagtatctc 240  
 tgatggtaga gggagagctc ataatcgtag aggacataat gatgggtgaag attctttgac 300

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```

tcatacagat gtcagctctt tccagacaat ggacccaaatg gtgtcaaata tgagaaacta 360
tatgcagaaa ttagaagaaa acttcgggtca actttcagtg gatccaaatg gacattcatt 420
ttgtttcttc tcagttatga cttattccaa aataggagat gaaccgccaa aggtttttca 480
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agattctgac agtggactag aaaaaatggc tattggtoat catatccatg accgagctca 600
tgtcattaaa aagtcaaaga acaagaagac tggagatgaa gaggtcaacc aggagtctcat 660
caatatgaat gaaagtgatg ctcatgcttt tgatgaggag tggcgaagtg aggttttgaa 720
gtacaaacca ggacgacaca atctaggaaa cactagaatg agaagtgttg gccatgagaa 780
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```

&lt;210&gt; 235

&lt;211&gt; 268

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 235

```

Met Phe Arg Met Leu Asn Ser Ser Phe Glu Asp Asp Pro Phe Phe Ser
  1             5             10             15

```

```

Glu Ser Ile Leu Ala His Arg Glu Asn Met Arg Gln Met Ile Arg Ser
      20             25             30

```

```

Phe Ser Glu Pro Phe Gly Arg Asp Leu Leu Ser Ile Ser Asp Gly Arg
      35             40             45

```

```

Gly Arg Ala His Asn Arg Arg Gly His Asn Asp Gly Glu Asp Ser Leu
      50             55             60

```

```

Thr His Thr Asp Val Ser Ser Phe Gln Thr Met Asp Gln Met Val Ser
      65             70             75             80

```

```

Asn Met Arg Asn Tyr Met Gln Lys Leu Glu Arg Asn Phe Gly Gln Leu
      85             90             95

```

```

Ser Val Asp Pro Asn Gly His Ser Phe Cys Ser Ser Ser Val Met Thr
      100            105            110

```

```

Tyr Ser Lys Ile Gly Asp Glu Pro Pro Lys Val Phe Gln Ala Ser Thr
      115            120            125

```

```

Gln Thr Arg Arg Ala Pro Gly Gly Ile Lys Glu Thr Arg Lys Ala Met
      130            135            140

```

```

Arg Asp Ser Asp Ser Gly Leu Glu Lys Met Ala Ile Gly His His Ile
      145            150            155            160

```

```

His Ser Arg Ala His Val Ile Lys Lys Ser Lys Asn Lys Lys Thr Gly
      165            170            175

```

```

Asp Glu Glu Val Asn Gln Glu Phe Ile Asn Met Asn Glu Ser Asp Ala
      180            185            190

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His Ala Phe Asp Glu Glu Trp Gln Ser Glu Val Leu Lys Tyr Lys Pro  
 195 200 205

Gly Arg His Asn Leu Gly Asn Thr Arg Met Arg Ser Val Gly His Glu  
 210 215 220

Asn Pro Gly Ser Arg Glu Leu Lys Arg Arg Glu Lys Pro Gln Gln Ser  
 225 230 235 240

Pro Ala Ile Glu His Gly Arg Arg Ser Asn Val Leu Gly Asp Lys Leu  
 245 250 255

His Ile Lys Gly Ser Ser Val Lys Ser Asn Lys Lys  
 260 265

&lt;210&gt; 236

&lt;211&gt; 1116

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 236

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 cgtttttcca atctgtccgc ggtcgcgcgc acccaagaca gagccagaat gttcaggatg 120  
 ctgaacagca gttttgagga tgaccccttc ttctctgagt ccattcttgc acaccgagaa 180  
 aatatcgac agatgataag aagtttttct gaacccttgc gaagagactt gctcagtatc 240  
 tctgatggta gagggagagc tcataatcgt agaggacata atgattgtga agattctttg 300  
 actcatcacg atgtcagctc ttccagacc atggaccaaa tgggtgtcaa tatgagaaac 360  
 tatatgcaga aattagaaag aaacttcggt caactttcag tggatccaaa tggacattca 420  
 tttgtttctt cctcagttat gacttattcc aaaataggag atgaaccgcc aaaggttttt 480  
 caggcctcaa ctcaaaactcg tcgagctcca ggaggaataa aggaaccagc gaaagcaatg 540  
 agagattctg acagtggaact agaaaaaatg gctattgggt atcatatcca tgaccgagct 600  
 catgtcatta aaaagtcaaa gaacaagaag actggagatg aagaggtcaa ccaggagttc 660  
 atcaatatga atgaaagcga tgctcatgct ttgatgagg agtggcaaa tgaggttttg 720  
 aagtacaac caggacgaca caatctagga aacactagaa tgagaagtgt tggccatgag 780  
 aatcctggct ccgcagaact taaaagaagg gagaaacctc aacaaagtcc agccattgaa 840  
 catgggaagg gatcaaatgt tttgggggac aaactccaca tcaaaaggctc atctgtgaaa 900  
 agcaacaaaa aataaaatagc catgcatttg atttgtttag ttttgattgt ttttaacagt 960  
 agtaatggtg ctgggtaata agcataagac caatctcttg ctgttaaatc agttctgtcc 1020  
 ttggcaactt tcttctgata tctgaatgtt catgaaggtc ctagctttat attgtccctc 1080  
 ttttaggaat aaaattttga ttttcaacaa aaaaaa 1116

&lt;210&gt; 237

&lt;211&gt; 86

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 237

Thr Thr Thr Ala Thr Leu Gly Phe Gly Ala Pro Gln Ala Pro Val Val  
 1 5 10 15

Asp Arg Glu Lys Gln Pro Ser Glu Gly Ala Phe Ser Glu Asn Asn Ala  
 20 25 30

Glu Asn Glu Ser Gly Gly Asp Lys Pro Pro Ile Asp Pro Asn Asn Pro  
 35 40 45

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Ala Ala Asn Trp Leu His Ala Arg Ser Thr Arg Lys Lys Arg Cys Pro  
 50 55 60

Tyr Thr Lys His Gln Thr Leu Glu Leu Glu Lys Glu Phe Leu Phe Asn  
 65 70 75 80

Met Tyr Leu Thr Arg Asp  
 85

&lt;210&gt; 238

&lt;211&gt; 258

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 238

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 aagcgggtgcc cctatacaaa acaccagacc ctggaactgg agaaagagtt tctgttcaac 240  
 atgtacctca ccaggagac 258

&lt;210&gt; 239

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 239

Met Ala Gly Phe Ser Pro Trp Arg Arg Arg Gln Arg Arg Arg Arg Arg  
 1 5 10 15

Arg Arg Arg Ala Arg His Ala Ser Arg Ala Ala Pro Glu Leu Val Gly  
 20 25 30

Asp Leu Gly Ser Phe Leu Leu Leu Gly Ser Thr Phe Leu Ser Thr Gly  
 35 40 45

Thr Thr Leu Pro Phe Ile Thr Ser Val Glu Ile Val Ser Arg Tyr Leu  
 50 55 60

Cys Ala Arg Gly Ser Gly Arg Ala Gly His His Gly Pro Gly Arg Ala  
 65 70 75 80

Arg Pro Ala Val Ala Thr Ser Ala Phe Pro Ala Gln Glu Pro Arg Val  
 85 90 95

Phe Leu Arg Ser Ala Leu Pro Ala Gly Arg Leu Ser Pro Ser Thr Thr  
 100 105 110

His Leu His Leu Val Thr Ala Asp Asn Pro Ala Ala Asn Trp Leu His  
 115 120 125

Ala Arg Ser Thr Arg Lys Lys Arg Cys Pro Tyr Thr Lys His Gln Thr  
 130 135 140

Leu Glu Leu Glu Lys Glu Phe Leu Phe Asn Met Tyr Leu Thr Arg Asp  
 145 150 155 160

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Arg Arg Tyr Glu Val Ala Arg Leu Leu Asn Leu Thr Glu Arg Gln Val  
165 170 175

Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Met Lys Lys Ile Asn Lys  
180 185 190

Asp Arg Ala Lys Asp Glu  
195

&lt;210&gt; 240

&lt;211&gt; 597

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 240

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cgaggtacg aggtggctcg actgctcaac ctaccgaga ggcaggtcaa gatctggttc 540  
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&lt;210&gt; 241

&lt;211&gt; 198

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 241

Met Ala Gly Phe Ser Pro Trp Arg Arg Arg Gln Arg Arg Arg Arg Arg  
1 5 10 15

Arg Arg Arg Ala Arg His Ala Ser Arg Ala Ala Pro Glu Leu Val Gly  
20 25 30

Asp Leu Gly Ser Phe Leu Leu Gly Ser Thr Phe Leu Ser Thr Gly  
35 40 45

Thr Thr Leu Pro Phe Ile Thr Ser Val Glu Ile Val Ser Arg Tyr Leu  
50 55 60

Cys Ala Arg Gly Ser Gly Arg Ala Gly His His Gly Pro Gly Arg Ala  
65 70 75 80

Arg Pro Ala Val Ala Thr Ser Ala Phe Pro Ala Gln Glu Pro Arg Val  
85 90 95

Phe Leu Arg Ser Ala Leu Pro Ala Gly Arg Leu Ser Pro Ser Thr Thr  
100 105 110

His Leu His Leu Val Thr Ala Asp Asn Pro Ala Ala Asn Trp Leu His  
115 120 125

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Ala Arg Ser Thr Arg Lys Lys Arg Cys Pro Tyr Thr Lys His Gln Thr  
 130 135 140

Leu Glu Leu Glu Lys Glu Phe Leu Phe Asn Met Tyr Leu Thr Arg Asp  
 145 150 155 160

Arg Arg Tyr Glu Val Ala Arg Leu Leu Asn Leu Thr Glu Arg Gln Val  
 165 170 175

Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Met Lys Lys Ile Asn Lys  
 180 185 190

Asp Arg Ala Lys Asp Glu  
 195

&lt;210&gt; 242

&lt;211&gt; 268

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 242

Met His His Trp Gly Leu Gly Asn Tyr Tyr Val Asp Ser Phe Leu Leu  
 1 5 10 15

Gly Ala Asp Ala Ala Asp Glu Leu Ser Val Gly Ala Met Arg Arg Gly  
 20 25 30

Pro Trp Pro Pro Pro Arg Gln Ala Ala Thr Leu Ala Glu His Pro Asp  
 35 40 45

Phe Ser Pro Cys Ser Phe Gln Ser Lys Ala Thr Val Phe Gly Ala Ser  
 50 55 60

Trp Asn Pro Val His Ala Arg Ala Pro Thr Leu Tyr Pro Leu Val Tyr  
 65 70 75 80

His His His His His His Pro Tyr Val His Pro Gln Ala Pro Trp Arg  
 85 90 95

Arg Gly Ala Asp Gly Arg Tyr Met Arg Ser Cys Trp Ser Pro Thr Pro  
 100 105 110

Gly Ala Leu Ser Phe Ala Gly Leu Pro Ser Ser Arg Pro Tyr Gly Ile  
 115 120 125

Lys Pro Glu Pro Leu Ser Ala Arg Arg Gly Asp Cys Pro Thr Leu Asp  
 130 135 140

Thr His Thr Phe Ser Leu Thr Asp Tyr Ala Cys Gly Ser Pro Pro Val  
 145 150 155 160

Asp Arg Glu Lys Gln Pro Ser Glu Gly Ala Phe Ser Glu Asn Asn Ala  
 165 170 175

Glu Asn Glu Ser Gly Gly Asp Lys Pro Pro Ile Asp Pro Asn Asn Pro  
 180 185 190

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Ala Ala Asn Trp Leu His Ala Arg Ser Thr Arg Lys Lys Arg Cys Pro  
195 200 205

Tyr Thr Lys His Gln Thr Leu Glu Leu Glu Lys Glu Phe Leu Phe Asn  
210 215 220

Met Tyr Leu Thr Arg Asp Arg Arg Tyr Glu Val Ala Arg Leu Leu Asn  
225 230 235 240

Leu Thr Glu Arg Gln Val Lys Ile Trp Phe Gln Asn Arg Arg Met Lys  
245 250 255

Met Lys Lys Ile Asn Lys Asp Arg Ala Lys Asp Glu  
260 265

&lt;210&gt; 243

&lt;211&gt; 6671

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 243

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&lt;210&gt; 244

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 244

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Arg Pro Met Pro Arg Leu Glu Pro Thr Phe Glu Ile Asp Glu Glu Glu
  1           5           10          15
Glu Glu Glu Asp Glu Asn Glu Leu Phe Pro Arg Glu Tyr Phe Arg Arg
          20          25          30
Leu Ser Ser Gln Asp Val Leu Arg Cys Gln Ser Ser Ser Lys Arg Lys
          35          40          45
Ser Lys Asp Glu Glu Glu Asp Glu Glu Ser Asp Asp Ala Asp Asp Gly
          50          55          60
Asn Asn Trp Glu His Lys Ser Ile Trp Thr Ala Leu
          65          70          75

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&lt;210&gt; 245

&lt;211&gt; 415

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 245

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&lt;210&gt; 246

&lt;211&gt; 68

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 246

Met Ala Glu Asn Leu Leu Asp Gly Pro Pro Asn Pro Lys Arg Ala Lys  
 1 5 10 15

Leu Ser Ser Pro Gly Phe Ser Ala Asn Asp Ser Thr Asp Thr Pro Ile  
 20 25 30

Leu Lys Pro Val Ser Leu Leu Arg Lys Arg Asp Val Lys Asn Ser Pro  
 35 40 45

Leu Glu Pro Asp Thr Ser Thr Pro Leu Lys Lys Lys Lys Gly Trp Pro  
 50 55 60

Lys Gly Lys Ser  
 65

&lt;210&gt; 247

&lt;211&gt; 229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 247

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 tacatccaca cctttgaaaa agaaaaaggg atggcccaaa ggcaagagc 229

&lt;210&gt; 248

&lt;211&gt; 376

&lt;212&gt; FRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 248

Arg Pro Met Pro Arg Leu Glu Pro Thr Phe Glu Ile Asp Glu Glu Glu  
 1 5 10 15

Glu Glu Glu Asp Glu Asn Glu Leu Phe Pro Arg Glu Tyr Phe Arg Arg  
 20 25 30

Leu Ser Ser Gln Asp Val Leu Arg Cys Gln Ser Ser Ser Lys Arg Lys  
 35 40 45

Ser Lys Asp Glu Glu Glu Asp Glu Glu Ser Asp Asp Ala Asp Asp Phe  
 50 55 60

Gly Ser Leu Phe Asp Leu Glu Asn Asp Leu Pro Asp Glu Leu Ile Pro  
 65 70 75 80

Asn Gly Gly Glu Leu Gly Leu Leu Asn Ser Gly Asn Leu Val Pro Asp  
 85 90 95

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Ala Ala Ser Lys His Lys Gln Leu Ser Glu Leu Leu Arg Gly Gly Ser  
 100 105 110

Gly Ser Ser Ile Asn Pro Gly Ile Gly Asn Val Ser Ala Ser Ser Pro  
 115 120 125

Val Gln Gln Gly Leu Gly Gly Gln Ala Gln Gly Gln Pro Asn Ser Ala  
 130 135 140

Asn Met Ala Ser Leu Ser Ala Met Gly Lys Ser Pro Leu Ser Gln Gly  
 145 150 155 160

Asp Ser Ser Ala Pro Ser Leu Pro Lys Gln Ala Ala Ser Thr Ser Gly  
 165 170 175

Pro Thr Pro Ala Ala Ser Gln Ala Leu Asn Pro Gln Ala Gln Lys Gln  
 180 185 190

Val Gly Leu Ala Thr Ser Ser Pro Ala Thr Ser Gln Thr Gly Pro Gly  
 195 200 205

Ile Cys Met Asn Ala Asn Phe Asn Gln Thr His Pro Gly Leu Leu Asn  
 210 215 220

Ser Asn Ser Gly His Ser Leu Ile Asn Gln Ala Ser Gln Gly Gln Ala  
 225 230 235 240

Gln Val Met Asn Gly Ser Leu Gly Ala Ala Gly Arg Gly Arg Gly Ala  
 245 250 255

Gly Met Pro Tyr Pro Thr Pro Ala Met Gln Gly Ala Ser Ser Ser Val  
 260 265 270

Leu Ala Glu Thr Leu Thr Gln Val Ser Pro Gln Met Thr Gly His Ala  
 275 280 285

Gly Leu Asn Thr Ala Gln Ala Gly Gly Met Ala Lys Met Gly Ile Thr  
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Gly Asn Thr Ser Pro Phe Gly Gln Pro Phe Ser Gln Ala Gly Gly Gln  
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Pro Met Gly Ala Thr Gly Val Asn Pro Gln Leu Ala Ser Lys Gln Ser  
 325 330 335

Met Val Asn Ser Leu Pro Thr Phe Pro Thr Asp Ile Lys Asn Thr Ser  
 340 345 350

Val Thr Asn Val Pro Asn Met Ser Gln Met Gln Thr Ser Val Gly Ile  
 355 360 365

Val Pro Thr Gln Ala Ile Ala Thr  
 370 375

&lt;210&gt; 249

&lt;211&gt; 1128

&lt;212&gt; DNA

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&lt;213&gt; Homo sapiens

&lt;400&gt; 249

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&lt;210&gt; 250

&lt;211&gt; 2004

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 250

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Ile Lys Lys Val Lys Lys Gln Lys Gln Arg Pro Ser Glu Glu Arg Ile
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Cys Asn Ala Val Ser Ser Ser His Gly Leu Asp Arg Lys Thr Val Leu
      35             40             45

Glu Gln Leu Glu Leu Ser Val Lys Asp Gly Thr Ile Leu Lys Val Ser
      50             55             60

Asn Lys Gly Leu Asn Ser Tyr Lys Asp Pro Asp Asn Pro Gly Arg Ile
      65             70             75             80

Ala Leu Pro Lys Pro Arg Asn His Gly Lys Leu Asp Asn Lys Gln Asn
      85             90             95

Val Asp Trp Asn Lys Leu Ile Lys Arg Ala Val Glu Gly Leu Ala Glu
      100            105            110

Ser Gly Gly Ser Thr Leu Lys Ser Ile Glu Arg Phe Leu Lys Gly Gln
      115            120            125

Lys Asp Val Ser Ala Leu Phe Gly Gly Ser Ala Ala Ser Gly Phe His
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Gln Gln Leu Arg Leu Ala Ile Lys Arg Ala Ile Gly His Gly Arg Leu

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Leu Lys Asp Gly Pro	Leu Tyr Arg	Leu Asn Thr Lys	Ala Thr Asn Val			
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Asp Gly Lys Glu Ser Cys	Glu Ser Leu Ser Cys	Leu Pro Pro Val Ser				
	180	185	190			
Leu Leu Pro His Glu Lys	Asp Lys Pro Val Ala	Glu Pro Ile Pro Ile				
	195	200	205			
Cys Ser Phe Cys Leu Gly	Thr Lys Glu Gln Asn	Arg Glu Lys Lys Pro				
	210	215	220			
Glu Glu Leu Ile Ser Cys	Ala Asp Cys Gly Asn	Ser Gly His Pro Ser				
	225	230	235		240	
Cys Leu Lys Phe Ser Pro	Glu Leu Thr Val Arg	Val Lys Ala Leu Arg				
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Trp Gln Cys Ile Glu Cys	Lys Thr Cys Ser Ser	Cys Arg Asp Gln Gly				
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Lys Asn Ala Asp Asn Met	Leu Phe Cys Asp Ser	Cys Asp Arg Gly Phe				
	275	280	285			
His Met Glu Cys Cys Asp	Pro Pro Leu Thr Arg	Met Pro Lys Gly Met				
	290	295	300			
Trp Ile Cys Gln Ile Cys	Arg Pro Arg Lys Lys	Gly Arg Lys Leu Leu				
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Gln Lys Lys Ala Ala Gln	Ile Lys Arg Arg Tyr	Thr Asn Pro Ile Gly				
	325	330	335			
Arg Pro Lys Asn Arg Leu	Lys Lys Gln Asn Thr	Val Ser Lys Gly Pro				
	340	345	350			
Phe Ser Lys Val Arg Thr	Gly Pro Gly Arg Gly	Arg Lys Arg Lys Ile				
	355	360	365			
Thr Leu Ser Ser Gln Ser	Ala Ser Ser Ser Ser	Glu Glu Gly Tyr Leu				
	370	375	380			
Glu Arg Ile Asp Gly Leu	Asp Phe Cys Arg Asp	Ser Asn Val Ser Leu				
	385	390	395		400	
Arg Phe Asn Lys Lys Thr	Lys Gly Leu Ile Asp	Gly Leu Thr Lys Phe				
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Phe Thr Pro Ser Pro Asp	Gly Arg Lys Ala Arg	Gly Glu Val Val Asp				
	420	425	430			
Tyr Ser Glu Gln Tyr Arg	Ile Arg Lys Arg Gly	Asn Arg Lys Ser Ser				
	435	440	445			
Thr Ser Asp Trp Pro Thr	Asp Asn Gln Asp Gly	Trp Asp Gly Lys Gln				
	450	455	460			

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 Asp Met Glu Leu Phe Arg Asp Ile Gln Glu Gln Ala Leu Gln Lys Val  
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 Glu Phe Gly Lys Tyr Glu Ile His Thr Trp Tyr Ser Ser Pro Tyr Pro  
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 Gly Trp Phe His Pro Pro Ala Asn Glu Ile Tyr Arg Lys Asn Asn Ile  
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 Ser Val Phe Glu Val Asp Gly Asn Val Ser Thr Ile Tyr Cys Gln Asn  
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 Gly Cys His Leu Val Gly Tyr Phe Ser Lys Glu Lys His Cys Gln Gln  
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 Lys Tyr Asn Val Ser Cys Ile Met Ile Leu Pro Gln Tyr Gln Arg Lys  
 645 650 655  
 Gly Tyr Gly Arg Phe Leu Ile Asp Phe Ser Tyr Leu Leu Ser Lys Arg  
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 Glu Gly Gln Ala Gly Ser Pro Glu Lys Pro Leu Ser Asp Leu Gly Arg  
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 Leu Asp Phe Arg Ser Asp Gln Phe Val Ile Ile Arg Arg Glu Lys Leu  
 740 745 750  
 Ile Gln Asp His Met Ala Lys Leu Gln Leu Asn Leu Arg Pro Val Asp  
 755 760 765

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 Lys Lys Pro Glu Val Met Ala Pro Val Ser Ser Thr Arg Leu Ser Lys  
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 Tyr Thr Glu Ser Glu Glu Gln Leu Val Ala Ser Glu Glu Gln Pro Ser  
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Lys Asp Glu Glu Glu Asp Glu Glu Ser Asp Asp Ala Asp Asp Thr Pro		
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Ile Leu Lys Pro Val Ser Leu Leu Arg Lys Arg Asp Val Lys Asn Ser		
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Pro Leu Glu Pro Asp Thr Ser Thr Pro Leu Lys Lys Lys Lys Gly Trp		
1140	1145	1150
Pro Lys Gly Lys Ser Arg Lys Pro Ile His Trp Lys Lys Arg Pro Gly		
1155	1160	1165
Arg Lys Pro Gly Phe Lys Leu Ser Arg Glu Ile Met Pro Val Ser Thr		
1170	1175	1180
Gln Ala Cys Val Ile Glu Pro Ile Val Ser Ile Pro Lys Ala Gly Arg		
1185	1190	1195
Lys Pro Lys Ile Gln Glu Ser Glu Glu Thr Val Glu Pro Lys Glu Asp		
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Met Pro Leu Pro Glu Glu Arg Lys Glu Glu Glu Glu Met Gln Ala Glu		
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Ala Glu Glu Ala Glu Glu Gly Glu Glu Glu Asp Ala Ala Ser Ser Glu		
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Val Pro Ala Ala Ser Pro Ala Asp Ser Ser Asn Ser Pro Glu Thr Glu		
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Thr Lys Glu Pro Glu Val Glu Glu Glu Glu Glu Lys Pro Arg Val Ser		
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Glu Glu Gln Arg Gln Ser Glu Glu Glu Gln Gln Glu Leu Glu Glu Pro		
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Glu Pro Glu Glu Glu Glu Asp Ala Ala Ala Glu Thr Ala Gln Asn Asp		
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Asp His Asp Ala Asp Asp Glu Asp Asp Gly His Leu Glu Ser Thr Lys		
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Lys Lys Glu Leu Glu Glu Gln Pro Thr Arg Glu Asp Val Lys Glu Glu		
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Pro Gly Val Gln Glu Ser Phe Leu Asp Ala Asn Met Gln Lys Ser Arg		
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Gln Pro Ser His Asp Thr Ser Val Val Ser Glu Gln Met Ala Gly Ser		
1380	1385	1390



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 Asp Cys His Ala Ser Glu His Asn Ser Pro Ile Ser Ser Val Gln Ser  
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 Tyr Asp Ser Thr Met Gly Gly Ser Ile Cys Gly Asn Ser Ser Ser Gln  
 1570 1575 1580  
 Ser Ser Cys Ser Tyr Gly Gly Leu Ser Ser Ser Ser Ser Leu Thr Gln  
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 Ser Met Met Gln Gln Ser Ser Val Gln Pro Ala Ala Asn Cys Ser Ile  
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 1685 1690 1695

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Gln Gln Gln Pro Pro Leu Ser Gln Cys Ser Met Asn Asn Ser Phe Thr  
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 1730 1735 1740  
 Ser Gln Pro Ser Ala Thr Phe Ser Leu Ala Lys Leu Gln Gln Leu Thr  
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 Gln Leu Tyr Gly Arg Ser Pro Ser Ala Val Ala Met Gln Ala Gly Pro  
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 Pro Thr Pro Ala Tyr Asn Val Asn Ser Met Asn Met Asn Thr Leu Asn  
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agccccatga	tggatgtgcc	ttccgtatca	gacctacttc	agcaggtggg	ggacagcgcc	5040
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gactccaaga	tggggcgagc	catctgtggg	aacagctctt	cccagagcag	ctgctctcac	5160
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gccagcatgg	gcagcagctg	cagcatgatg	cagcagagca	gcgtccagcc	tgctgccaac	5280
tgcagatcat	agtcacctca	gagctgcgtg	gtggagaggg	ctcccagtaa	ccagcagcag	5340
cagccgccac	caccgcctcc	acagcagcca	cagccgcgcg	gcgccacaac	caaccacgca	5400
ccacagctcc	caccacccca	gcagcagccg	caacagcagc	cgcagctcca	gccccagcag	5460
cctccaccct	cacccccctc	ccagcagcag	cccccgctgt	cacagtgtag	tatgaataac	5520
agttcttacc	cagctcctat	gatcatggag	ataccagaa	ctggaaagca	tgggaacata	5580
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ccttatagcc	atctctctgc	tgtgaattcc	tatgcaacca	gtgtttctct	gtccaatata	5760
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gcactggctg	ttcagcgtgg	catgaacatg	ggggttaate	tgatgcctac	tcccctctat	6120
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cccatgtatga	acagcagttg	ccatgatga	ccctgcatac	tgaaccagca	agcagcagat	6240
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cttaaccctc	atgggaacat	gatgtacaca	ggccctctcc	ctacacagct	ctcgaagcgt	6360
gctggcgtgc	ccaagcagtc	actcaacgga	ccttcatatga	gaagatgagc	aagatgaact	6420
tgcatacaaa	aacttaataa	tataataata	aaggaaacct	tactactgac	aaaccagaga	6480

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ttggtttttct tcaaatctct gaacatttta cagtagaact catctaaaaa tggatttggg 6660
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atagacggagc ttacttgaaa tctttgttgt tcttgaatca agtgaatat atgttttttc 7140
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7869

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&lt;210&gt; 252

&lt;211&gt; 2442

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 252

```

Met Ala Glu Asn Leu Leu Asp Gly Pro Pro Asn Pro Lys Arg Ala Lys
1 5 10 15

```

```

Leu Ser Ser Pro Gly Phe Ser Ala Asn Asp Ser Thr Asp Phe Gly Ser
20 25 30

```

```

Leu Phe Asp Leu Glu Asn Asp Leu Pro Asp Glu Leu Ile Pro Asn Gly
35 40 45

```

```

Gly Glu Leu Gly Leu Leu Asn Ser Gly Asn Leu Val Pro Asp Ala Ala
50 55 60

```

```

Ser Lys His Lys Gln Leu Ser Glu Leu Leu Arg Gly Gly Ser Gly Ser
65 70 75 80

```

```

Ser Ile Asn Pro Gly Ile Gly Asn Val Ser Ala Ser Ser Pro Val Gln
85 90 95

```

```

Gln Gly Leu Gly Gly Gln Ala Gln Gly Gln Pro Asn Ser Ala Asn Met
100 105 110

```

```

Ala Ser Leu Ser Ala Met Gly Lys Ser Pro Leu Ser Gln Gly Asp Ser
115 120 125

```

```

Ser Ala Pro Ser Leu Pro Lys Gln Ala Ala Ser Thr Ser Gly Pro Thr
130 135 140

```

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Pro Ala Ala Ser Gln Ala Leu Asn Pro Gln Ala Gln Lys Gln Val Gly  
 145 150 155 160  
 Leu Ala Thr Ser Ser Pro Ala Thr Ser Gln Thr Gly Pro Gly Ile Cys  
 165 170 175  
 Met Asn Ala Asn Phe Asn Gln Thr His Pro Gly Leu Leu Asn Ser Asn  
 180 185 190  
 Ser Gly His Ser Ser Leu Ile Asn Gln Ala Ser Gln Gly Gln Ala Gln Val  
 195 200 205  
 Met Asn Gly Ser Leu Gly Ala Ala Gly Arg Gly Arg Gly Ala Gly Met  
 210 215 220  
 Pro Tyr Pro Thr Pro Ala Met Gln Gly Ala Ser Ser Ser Val Leu Ala  
 225 230 235 240  
 Glu Thr Leu Thr Gln Val Ser Pro Gln Met Thr Gly His Ala Gly Leu  
 245 250 255  
 Asn Thr Ala Gln Ala Gly Gly Met Ala Lys Met Gly Ile Thr Gly Asn  
 260 265 270  
 Thr Ser Pro Phe Gly Gln Pro Phe Ser Gln Ala Gly Gly Gln Pro Met  
 275 280 285  
 Gly Ala Thr Gly Val Asn Pro Gln Leu Ala Ser Lys Gln Ser Met Val  
 290 295 300  
 Asn Ser Leu Pro Thr Phe Pro Thr Asp Ile Lys Asn Thr Ser Val Thr  
 305 310 315 320  
 Asn Val Pro Asn Met Ser Gln Met Gln Thr Ser Val Gly Ile Val Pro  
 325 330 335  
 Thr Gln Ala Ile Ala Thr Gly Pro Thr Ala Asp Pro Glu Lys Arg Lys  
 340 345 350  
 Leu Ile Gln Gln Gln Leu Val Leu Leu Leu His Ala His Lys Cys Gln  
 355 360 365  
 Arg Arg Glu Gln Ala Asn Gly Glu Val Arg Ala Cys Ser Leu Pro His  
 370 375 380  
 Cys Arg Thr Met Lys Asn Val Leu Asn His Met Thr His Cys Gln Ala  
 385 390 395 400  
 Gly Lys Ala Cys Gln Val Ala His Cys Ala Ser Ser Arg Gln Ile Ile  
 405 410 415  
 Ser His Trp Lys Asn Cys Thr Arg His Asp Cys Pro Val Cys Leu Pro  
 420 425 430  
 Leu Lys Asn Ala Ser Asp Lys Arg Asn Gln Gln Thr Ile Leu Gly Ser  
 435 440 445

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Pro Ala Ser Gly Ile Gln Asn Thr Ile Gly Ser Val Gly Thr Gly Gln  
 450 455 460  
 Gln Asn Ala Thr Ser Leu Ser Asn Pro Asn Pro Ile Asp Pro Ser Ser  
 465 470 475 480  
 Met Gln Arg Ala Tyr Ala Ala Leu Gly Leu Pro Tyr Met Asn Gln Pro  
 485 490 495  
 Gln Thr Gln Leu Gln Pro Gln Val Pro Gly Gln Gln Pro Ala Gln Pro  
 500 505 510  
 Gln Thr His Gln Gln Met Arg Thr Leu Asn Pro Leu Gly Asn Asn Pro  
 515 520 525  
 Met Asn Ile Pro Ala Gly Gly Ile Thr Thr Asp Gln Gln Pro Pro Asn  
 530 535 540  
 Leu Ile Ser Glu Ser Ala Leu Pro Thr Ser Leu Gly Ala Thr Asn Pro  
 545 550 555 560  
 Leu Met Asn Asp Gly Ser Asn Ser Gly Asn Ile Gly Thr Leu Ser Thr  
 565 570 575  
 Ile Pro Thr Ala Ala Pro Pro Ser Ser Thr Gly Val Arg Lys Gly Trp  
 580 585 590  
 His Glu His Val Thr Gln Asp Leu Arg Ser His Leu Val His Lys Leu  
 595 600 605  
 Val Gln Ala Ile Phe Pro Thr Pro Asp Pro Ala Ala Leu Lys Asp Arg  
 610 615 620  
 Arg Met Glu Asn Leu Val Ala Tyr Ala Lys Lys Val Glu Gly Asp Met  
 625 630 635 640  
 Tyr Glu Ser Ala Asn Ser Arg Asp Glu Tyr Tyr His Leu Leu Ala Glu  
 645 650 655  
 Lys Ile Tyr Lys Ile Gln Lys Glu Leu Glu Glu Lys Arg Arg Ser Arg  
 660 665 670  
 Leu His Lys Gln Gly Ile Leu Gly Asn Gln Pro Ala Leu Pro Ala Pro  
 675 680 685  
 Gly Ala Gln Pro Pro Val Ile Pro Gln Ala Gln Pro Val Arg Pro Pro  
 690 695 700  
 Asn Gly Pro Leu Ser Leu Pro Val Asn Arg Met Gln Val Ser Gln Gly  
 705 710 715 720  
 Met Asn Ser Phe Asn Pro Met Ser Leu Gly Asn Val Gln Leu Pro Gln  
 725 730 735  
 Ala Pro Met Gly Pro Arg Ala Ala Ser Pro Met Asn His Ser Val Gln  
 740 745 750  
 Met Asn Ser Met Gly Ser Val Pro Gly Met Ala Ile Ser Pro Ser Arg

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755	760	765
Met Pro Gln Pro Pro Asn Met Met Gly Ala His Thr Asn Asn Met Met		
770	775	780
Ala Gln Ala Pro Ala Gln Ser Gln Phe Leu Pro Gln Asn Gln Phe Pro		
785	790	800
Ser Ser Ser Gly Ala Met Ser Val Gly Met Gly Gln Pro Pro Ala Gln		
805	810	815
Thr Gly Val Ser Gln Gly Gln Val Pro Gly Ala Ala Leu Pro Asn Pro		
820	825	830
Leu Asn Met Leu Gly Pro Gln Ala Ser Gln Leu Pro Cys Pro Pro Val		
835	840	845
Thr Gln Ser Pro Leu His Pro Thr Pro Pro Pro Ala Ser Thr Ala Ala		
850	855	860
Gly Met Pro Ser Leu Gln His Thr Thr Pro Pro Gly Met Thr Pro Pro		
865	870	875
Gln Pro Ala Ala Pro Thr Gln Pro Ser Thr Pro Val Ser Ser Ser Gly		
885	890	895
Gln Thr Pro Thr Pro Thr Pro Gly Ser Val Pro Ser Ala Thr Gln Thr		
900	905	910
Gln Ser Thr Pro Thr Val Gln Ala Ala Ala Gln Ala Gln Val Thr Pro		
915	920	925
Gln Pro Gln Thr Pro Val Gln Pro Pro Ser Val Ala Thr Pro Gln Ser		
930	935	940
Ser Gln Gln Gln Pro Thr Pro Val His Ala Gln Pro Pro Gly Thr Pro		
945	950	955
Leu Ser Gln Ala Ala Ala Ser Ile Asp Asn Arg Val Pro Thr Pro Ser		
965	970	975
Ser Val Ala Ser Ala Glu Thr Asn Ser Gln Gln Pro Gly Pro Asp Val		
980	985	990
Pro Val Leu Glu Met Lys Thr Glu Thr Gln Ala Glu Asp Thr Glu Pro		
995	1000	1005
Asp Pro Gly Glu Ser Lys Gly Glu Pro Arg Ser Glu Met Met Glu Glu		
1010	1015	1020
Asp Leu Gln Gly Ala Ser Gln Val Lys Glu Glu Thr Asp Ile Ala Glu		
1025	1030	1035
Gln Lys Ser Glu Pro Met Glu Val Asp Glu Lys Lys Pro Glu Val Lys		
1045	1050	1055
Val Glu Val Lys Glu Glu Glu Glu Ser Ser Asn Gly Thr Ala Ser		
1060	1065	1070



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Gln Ser Thr Ser Pro Ser Gln Pro Arg Lys Lys Ile Phe Lys Pro Glu  
 1075 1080 1085

Glu Leu Arg Gln Ala Leu Met Pro Thr Leu Glu Ala Leu Tyr Arg Gln  
 1090 1095 1100

Asp Pro Glu Ser Leu Pro Phe Arg Gln Pro Val Asp Pro Gln Leu Leu  
 1105 1110 1115 1120

Gly Ile Pro Asp Tyr Phe Asp Ile Val Lys Asn Pro Met Asp Leu Ser  
 1125 1130 1135

Thr Ile Lys Arg Lys Leu Asp Thr Gly Gln Tyr Gln Glu Pro Trp Gln  
 1140 1145 1150

Tyr Val Asp Asp Val Trp Leu Met Phe Asn Asn Ala Trp Leu Tyr Asn  
 1155 1160 1165

Arg Lys Thr Ser Arg Val Tyr Lys Phe Cys Ser Lys Leu Ala Glu Val  
 1170 1175 1180

Phe Glu Gln Glu Ile Asp Pro Val Met Gln Ser Leu Gly Tyr Cys Cys  
 1185 1190 1195 1200

Gly Arg Lys Tyr Glu Phe Ser Pro Gln Thr Leu Cys Cys Tyr Gly Lys  
 1205 1210 1215

Gln Leu Cys Thr Ile Pro Arg Asp Ala Ala Tyr Tyr Ser Tyr Gln Asn  
 1220 1225 1230

Arg Tyr His Phe Cys Glu Lys Cys Phe Thr Glu Ile Gln Gly Glu Asn  
 1235 1240 1245

Val Thr Leu Gly Asp Asp Pro Ser Gln Pro Gln Thr Thr Ile Ser Lys  
 1250 1255 1260

Asp Gln Phe Glu Lys Lys Lys Asn Asp Thr Leu Asp Pro Glu Pro Phe  
 1265 1270 1275 1280

Val Asp Cys Lys Glu Cys Gly Arg Lys Met His Gln Ile Cys Val Leu  
 1285 1290 1295

His Tyr Asp Ile Ile Trp Pro Ser Gly Phe Val Cys Asp Asn Cys Leu  
 1300 1305 1310

Lys Lys Thr Gly Arg Pro Arg Lys Glu Asn Lys Phe Ser Ala Lys Arg  
 1315 1320 1325

Leu Gln Thr Thr Arg Leu Gly Asn His Leu Glu Asp Arg Val Asn Lys  
 1330 1335 1340

Phe Leu Arg Arg Gln Asn His Pro Glu Ala Gly Glu Val Phe Val Arg  
 1345 1350 1355 1360

Val Val Ala Ser Ser Asp Lys Thr Val Glu Val Lys Pro Gly Met Lys  
 1365 1370 1375

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Ser Arg Phe Val Asp Ser Gly Glu Met Ser Glu Ser Phe Pro Tyr Arg  
 1380 1385 1390  
 Thr Lys Ala Leu Phe Ala Phe Glu Glu Ile Asp Gly Val Asp Val Cys  
 1395 1400 1405  
 Phe Phe Gly Met His Val Gln Glu Tyr Gly Ser Asp Cys Pro Pro Pro  
 1410 1415 1420  
 Asn Thr Arg Arg Val Tyr Ile Ser Tyr Leu Asp Ser Ile His Phe Phe  
 1425 1430 1435 1440  
 Arg Pro Arg Cys Leu Arg Thr Ala Val Tyr His Glu Ile Leu Ile Gly  
 1445 1450 1455  
 Tyr Leu Glu Tyr Val Lys Lys Leu Gly Tyr Val Thr Gly His Ile Trp  
 1460 1465 1470  
 Ala Cys Pro Pro Ser Glu Gly Asp Asp Tyr Ile Phe His Cys His Pro  
 1475 1480 1485  
 Pro Asp Gln Lys Ile Pro Lys Pro Lys Arg Leu Gln Glu Trp Tyr Lys  
 1490 1495 1500  
 Lys Met Leu Asp Lys Ala Phe Ala Glu Arg Ile Ile His Asp Tyr Lys  
 1505 1510 1515 1520  
 Asp Ile Phe Lys Gln Ala Thr Glu Asp Arg Leu Thr Ser Ala Lys Glu  
 1525 1530 1535  
 Leu Pro Tyr Phe Glu Gly Asp Phe Trp Pro Asn Val Leu Glu Glu Ser  
 1540 1545 1550  
 Ile Lys Glu Leu Glu Gln Glu Glu Glu Arg Lys Lys Glu Glu Ser  
 1555 1560 1565  
 Thr Ala Ala Ser Glu Thr Thr Glu Gly Ser Gln Gly Asp Ser Lys Asn  
 1570 1575 1580  
 Ala Lys Lys Lys Asn Asn Lys Lys Thr Asn Lys Asn Lys Ser Ser Ile  
 1585 1590 1595 1600  
 Ser Arg Ala Asn Lys Lys Lys Pro Ser Met Pro Asn Val Ser Asn Asp  
 1605 1610 1615  
 Leu Ser Gln Lys Leu Tyr Ala Thr Met Glu Lys His Lys Glu Val Phe  
 1620 1625 1630  
 Phe Val Ile His Leu His Ala Gly Pro Val Ile Asn Thr Leu Pro Pro  
 1635 1640 1645  
 Ile Val Asp Pro Asp Pro Leu Leu Ser Cys Asp Leu Met Asp Gly Arg  
 1650 1655 1660  
 Asp Ala Phe Leu Thr Leu Ala Arg Asp Lys His Trp Glu Phe Ser Ser  
 1665 1670 1675 1680  
 Leu Arg Arg Ser Lys Trp Ser Thr Leu Cys Met Leu Val Glu Leu His

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1685	1690	1695
Thr Gln Gly Gln Asp Arg Phe Val Tyr Thr Cys Asn Glu Cys Lys His 1700	1705	1710
His Val Glu Thr Arg Trp His Cys Thr Val Cys Glu Asp Tyr Asp Leu 1715	1720	1725
Cys Ile Asn Cys Tyr Asn Thr Lys Ser His Ala His Lys Met Val Lys 1730	1735	1740
Trp Gly Leu Gly Leu Asp Asp Glu Gly Ser Ser Gln Gly Glu Pro Gln 1745	1750	1755
Ser Lys Ser Pro Gln Glu Ser Arg Arg Leu Ser Ile Gln Arg Cys Ile 1765	1770	1775
Gln Ser Leu Val His Ala Cys Gln Cys Arg Asn Ala Asn Cys Ser Leu 1780	1785	1790
Pro Ser Cys Gln Lys Met Lys Arg Val Val Gln His Thr Lys Gly Cys 1795	1800	1805
Lys Arg Lys Thr Asn Gly Gly Cys Pro Val Cys Lys Gln Leu Ile Ala 1810	1815	1820
Leu Cys Cys Tyr His Ala Lys His Cys Gln Glu Asn Lys Cys Pro Val 1825	1830	1835
Pro Phe Cys Leu Asn Ile Lys His Lys Leu Arg Gln Gln Gln Ile Gln 1845	1850	1855
His Arg Leu Gln Gln Ala Gln Leu Met Arg Arg Arg Met Ala Thr Met 1860	1865	1870
Asn Thr Arg Asn Val Pro Gln Gln Ser Leu Pro Ser Pro Thr Ser Ala 1875	1880	1885
Pro Pro Gly Thr Pro Thr Gln Gln Pro Ser Thr Pro Gln Thr Pro Gln 1890	1895	1900
Pro Pro Ala Gln Pro Gln Pro Ser Pro Val Ser Met Ser Pro Ala Gly 1905	1910	1915
Phe Pro Ser Val Ala Arg Thr Gln Pro Pro Thr Thr Val Ser Thr Gly 1925	1930	1935
Lys Pro Thr Ser Gln Val Pro Ala Pro Pro Pro Pro Ala Gln Pro Pro 1940	1945	1950
Pro Ala Ala Val Glu Ala Ala Arg Gln Ile Glu Arg Glu Ala Gln Gln 1955	1960	1965
Gln Gln His Leu Tyr Arg Val Asn Ile Asn Asn Ser Met Pro Pro Gly 1970	1975	1980
Arg Thr Gly Met Gly Thr Pro Gly Ser Gln Met Ala Pro Val Ser Leu 1985	1990	2000

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Asn Val Pro Arg Pro Asn Gln Val Ser Gly Pro Val Met Pro Ser Met  
 2005 2010 2015  
 Pro Pro Gly Gln Trp Gln Gln Ala Pro Leu Pro Gln Gln Gln Pro Met  
 2020 2025 2030  
 Pro Gly Leu Pro Arg Pro Val Ile Ser Met Gln Ala Gln Ala Ala Val  
 2035 2040 2045  
 Ala Gly Pro Arg Met Pro Ser Val Gln Pro Pro Arg Ser Ile Ser Pro  
 2050 2055 2060  
 Ser Ala Leu Gln Asp Leu Leu Arg Thr Leu Lys Ser Pro Ser Ser Pro  
 2065 2070 2075 2080  
 Gln Gln Gln Gln Val Leu Asn Ile Leu Lys Ser Asn Pro Gln Leu  
 2085 2090 2095  
 Met Ala Ala Phe Ile Lys Gln Arg Thr Ala Lys Tyr Val Ala Asn Gln  
 2100 2105 2110  
 Pro Gly Met Gln Pro Gln Pro Gly Leu Gln Ser Gln Pro Gly Met Gln  
 2115 2120 2125  
 Pro Gln Pro Gly Met His Gln Gln Pro Ser Leu Gln Asn Leu Asn Ala  
 2130 2135 2140  
 Met Gln Ala Gly Val Pro Arg Pro Gly Val Pro Pro Gln Gln Gln Ala  
 2145 2150 2155 2160  
 Met Gly Gly Leu Asn Pro Gln Gly Gln Ala Leu Asn Ile Met Asn Pro  
 2165 2170 2175  
 Gly His Asn Pro Asn Met Ala Ser Met Asn Pro Gln Tyr Arg Glu Met  
 2180 2185 2190  
 Leu Arg Arg Gln Leu Leu Gln Gln Gln Gln Gln Gln Gln Gln  
 2195 2200 2205  
 Gln Gln Gln Gln Gln Gln Gln Gln Gly Ser Ala Gly Met Ala Gly Gly  
 2210 2215 2220  
 Met Ala Gly His Gly Gln Phe Gln Gln Pro Gln Gly Pro Gly Gly Tyr  
 2225 2230 2235 2240  
 Pro Pro Ala Met Gln Gln Gln Gln Arg Met Gln Gln His Leu Pro Leu  
 2245 2250 2255  
 Gln Gly Ser Ser Met Gly Gln Met Ala Ala Gln Met Gly Gln Leu Gly  
 2260 2265 2270  
 Gln Met Gly Gln Pro Gly Leu Gly Ala Asp Ser Thr Pro Asn Ile Gln  
 2275 2280 2285  
 Gln Ala Leu Gln Gln Arg Ile Leu Gln Gln Gln Gln Met Lys Gln Gln  
 2290 2295 2300

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Ile Gly Ser Pro Gly Gln Pro Asn Pro Met Ser Pro Gln Gln His Met  
 2305 2310 2315 2320

Leu Ser Gly Gln Pro Gln Ala Ser His Leu Pro Gly Gln Gln Ile Ala  
 2325 2330 2335

Thr Ser Leu Ser Asn Gln Val Arg Ser Pro Ala Pro Val Gln Ser Pro  
 2340 2345 2350

Arg Pro Gln Ser Gln Pro Pro His Ser Ser Pro Ser Pro Arg Ile Gln  
 2355 2360 2365

Pro Gln Pro Ser Pro His His Val Ser Pro Gln Thr Gly Ser Pro His  
 2370 2375 2380

Pro Gly Leu Ala Val Thr Met Ala Ser Ser Ile Asp Gln Gly His Leu  
 2385 2390 2395 2400

Gly Asn Pro Glu Gln Ser Ala Met Leu Pro Gln Leu Asn Thr Pro Ser  
 2405 2410 2415

Arg Ser Ala Leu Ser Ser Glu Leu Ser Leu Val Gly Asp Thr Thr Gly  
 2420 2425 2430

Asp Thr Leu Glu Lys Phe Val Glu Gly Leu  
 2435 2440

&lt;210&gt; 253

&lt;211&gt; 8147

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 253

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 ccccgctccg ccgcggccgc cgcctccgc cgccctccgc cgcgccccc ggccgcccc 180  
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 cagccggccc cgccggcgcc gcgcggcgcc cgccggcgcc ccaccgcgga gtgtcgccgt 540  
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 cgcgcctcgc cctccctct cctcggcgcc cgcccgcgcc cgtcgcgcgc gcccgcgctc 720  
 gctcctctcc ctgcgcgcgc gcagggcccc cgaccgccgt ccgggccctc gccggccggg 780  
 cgcgcgcgtc cgccggcggt ttctcgcgag aggtgaaat ggctgagaac ttgctggacc 840  
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 acagtctctaa catggccagc ctcaagtcca tgggcaagag cctctgagc caggagatt 1200  
 ctacagcccc cagcctgcct aaacaggcag ccagcacctc tggggccacc ccgctgcct 1260  
 cccaagcact gaatccgcaa gcacaaaagc aagtggggt ggcgactagc agccttgca 1320  
 cgtcacagac tggacctggt atctgcatga atgctaactt taaccagacc caccagagcc 1380  
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cgcgaatgac	tggtcacgcg	ggactgaaca	cgcacagggc	agcaggcatg	ccaagatggg	1620
gaataactgg	gaacacaaat	ccatttggac	agccctttag	tcaagctgga	ggggcagcaa	1680
tgggagccac	tgagatgaac	ccccagttag	ccagcaaaaca	gagcatggtc	aacagtttgc	1740
ccacctctccc	tacagatatt	aagaatactt	cagtcaccaa	cgtgcacaa	atgtctcaga	1800
tgcacaacatc	agtggtgaatt	gtaccacac	aagcaattgc	aacaggcccc	actgcagatc	1860
ctgaaaaaacg	caaacgtata	cagcagcagc	tggttctact	gcttcctatg	cataagtgct	1920
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<210> 254

<211> 183

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&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 254

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Tyr Thr Pro Pro Glu Ser Pro Val Pro Ser Tyr Ala Ser Ser Thr Pro
 20             25             30

Leu His Val Pro Val Pro Arg Ala Leu Arg Met Glu Glu Asp Ser Ile
 35             40             45

Arg Leu Pro Ala His Leu Arg Leu Gln Pro Ile Tyr Trp Ser Arg Asp
 50             55             60

Asp Val Ala Gln Trp Leu Lys Trp Ala Glu Asn Glu Phe Ser Leu Arg
 65             70             75

Pro Ile Asp Ser Asn Thr Phe Glu Met Asn Gly Lys Ala Leu Leu Leu
 85             90             95

Leu Thr Lys Glu Asp Phe Arg Tyr Arg Ser Pro His Ser Gly Asp Val
100             105             110

Leu Tyr Glu Leu Leu Gln His Ile Leu Lys Gln Arg Lys Pro Arg Ile
115             120             125

Leu Phe Ser Pro Phe Phe His Pro Gly Asn Ser Ile His Thr Gln Pro
130             135             140

Glu Val Ile Leu His Gln Asn His Glu Glu Glu Ala Leu Gln Arg Pro
145             150             155             160

Val Ala Ser Asp Phe Glu Pro Gln Gly Leu Ser Glu Ala Ala Arg Trp
165             170             175

Asn Ser Lys Glu Asn Leu Leu
180

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&lt;210&gt; 255

&lt;211&gt; 549

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 255

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<210> 256  
 <211> 763  
 <212> DNA  
 <213> Homo sapiens

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<400> 256
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<210> 257  
 <211> 604  
 <212> DNA  
 <213> Homo sapiens

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<400> 257
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tctgtgaact gaactcttct tgaacttttt gtgtgtgttg ttattgttgc ttttggagat 180
agggtcttgc tctgtcaccg aggcctggact gcagtggcac aatcacagct cactgcagcc 240
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gcataatgcta cctgactaat taaaaatttt tttttttttt tgtagagaca gggctcact 360
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gctt 604

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<210> 258  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

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<400> 258
Arg Tyr Arg Ser Pro His Ser Ala His Asp Leu Pro Ala Asn Lys
1           5           10          15

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<210> 259  
 <211> 45  
 <212> DNA  
 <213> Homo sapiens

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<400> 259
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45

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<210> 260  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 260  
Ile Arg Leu Pro Ala His Leu Pro His Asp Leu Pro Ala Asn Lys  
1 5 10 15

<210> 261  
<211> 45  
<212> DNA  
<213> Homo sapiens

<400> 261  
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<210> 262  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 262  
Gln Asn Pro Asn Ser Lys Glu Gly Asp Val Leu Tyr Glu Leu Leu  
1 5 10 15

<210> 263  
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<212> DNA  
<213> Homo sapiens

<400> 263  
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<210> 264  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 264  
Gln Asn Pro Asn Ser Lys Glu Gly Leu Gln Pro Ile Tyr Trp Ser  
1 5 10 15

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<211> 45  
<212> DNA  
<213> Homo sapiens

<400> 265  
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212/299

&lt;210&gt; 266

&lt;211&gt; 829

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 266

Met Asn Ser Gly Val Ala Met Lys Tyr Gly Asn Asp Ser Ser Ala Glu  
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Leu Ser Glu Leu His Ser Ala Ala Leu Ala Ser Leu Lys Gly Asp Ile  
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Val Glu Leu Asn Lys Arg Leu Gln Gln Thr Glu Arg Glu Arg Asp Leu  
 35 40 45

Leu Glu Lys Lys Leu Ala Lys Ala Gln Cys Glu Gln Ser His Leu Met  
 50 55 60

Arg Glu His Glu Asp Val Gln Glu Arg Thr Thr Leu Arg Tyr Glu Glu  
 65 70 75 80

Arg Ile Thr Glu Leu His Ser Val Ile Ala Glu Leu Asn Lys Lys Ile  
 85 90 95

Asp Arg Leu Gln Gly Thr Thr Ile Arg Glu Glu Asp Glu Tyr Ser Glu  
 100 105 110

Leu Arg Ser Glu Leu Ser Gln Ser Gln His Glu Val Asn Glu Asp Ser  
 115 120 125

Arg Ser Met Asp Gln Asp Gln Thr Ser Val Ser Ile Pro Glu Asn Gln  
 130 135 140

Ser Thr Met Val Thr Ala Asp Met Asp Asn Cys Ser Asp Leu Asn Ser  
 145 150 155 160

Glu Leu Gln Arg Val Leu Thr Gly Leu Glu Asn Val Val Cys Gly Arg  
 165 170 175

Lys Lys Ser Ser Cys Ser Leu Ser Val Ala Glu Val Asp Arg His Ile  
 180 185 190

Glu Gln Leu Thr Thr Ala Ser Glu His Cys Asp Leu Ala Ile Lys Thr  
 195 200 205

Val Glu Glu Ile Glu Gly Val Leu Gly Arg Asp Leu Tyr Pro Asn Leu  
 210 215 220

Ala Glu Glu Arg Ser Arg Trp Glu Lys Glu Leu Ala Gly Leu Arg Glu  
 225 230 235 240

Glu Asn Glu Ser Leu Thr Ala Met Leu Cys Ser Lys Glu Glu Glu Leu  
 245 250 255

Asn Arg Thr Lys Ala Thr Met Asn Ala Ile Arg Glu Glu Arg Asp Arg  
 260 265 270

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Leu Arg Arg Arg Val Arg Glu Leu Gln Thr Arg Leu Gln Ser Val Gln  
 275 280 285  
 Ala Thr Gly Pro Ser Ser Pro Gly Arg Leu Thr Ser Thr Asn Arg Pro  
 290 295 300  
 Ile Asn Pro Ser Thr Gly Glu Leu Ser Thr Ser Ser Ser Ser Asn Asp  
 305 310 315 320  
 Ile Pro Ile Ala Lys Ile Ala Glu Arg Val Lys Leu Ser Lys Thr Arg  
 325 330 335  
 Ser Glu Ser Ser Ser Ser Asp Arg Pro Val Leu Gly Ser Glu Ile Ser  
 340 345 350  
 Ser Ile Gly Val Ser Ser Ser Val Ala Glu His Leu Ala His Ser Leu  
 355 360 365  
 Gln Asp Cys Ser Asn Ile Gln Glu Ile Phe Gln Thr Leu Tyr Ser His  
 370 375 380  
 Gly Ser Ala Ile Ser Glu Ser Lys Ile Arg Glu Phe Glu Val Glu Thr  
 385 390 395 400  
 Glu Arg Leu Asn Ser Arg Ile Glu His Leu Lys Ser Gln Asn Asp Leu  
 405 410 415  
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 420 425 430  
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 435 440 445  
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 465 470 475 480  
 Gly Val Gly Ser Ser Pro Gly Asp Gln Ser Gly Asp Glu Asn Ile Thr  
 485 490 495  
 Gln Met Leu Lys Arg Ala His Asp Cys Arg Lys Thr Ala Glu Asn Ala  
 500 505 510  
 Ala Lys Ala Leu Leu Met Lys Leu Asp Gly Ser Cys Gly Gly Ala Phe  
 515 520 525  
 Ala Val Ala Gly Cys Ser Val Gln Pro Trp Glu Ser Leu Ser Ser Asn  
 530 535 540  
 Ser His Thr Ser Thr Thr Ser Ser Thr Ala Ser Ser Cys Asp Thr Glu  
 545 550 555 560  
 Phe Thr Lys Glu Asp Glu Gln Arg Leu Lys Asp Tyr Ile Gln Gln Leu  
 565 570 575  
 Lys Asn Asp Arg Ala Ala Val Lys Leu Thr Met Leu Glu Leu Glu Ser

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Val	Gln	Glu	Leu	Val	Ser	Ala	Leu	Glu	Arg	Leu	Thr	Lys	Ser	Ser	Glu				
740										745					750				
Ile	Arg	His	Gln	Gln	Ser	Ala	Glu	Phe	Val	Asn	Asp	Leu	Lys	Arg	Ala				
755										760					765				
Asn	Ser	Asn	Leu	Val	Ala	Ala	Tyr	Glu	Lys	Ala	Lys	Lys	Lys	His	Gln				
770										775					780				
Asn	Lys	Leu	Lys	Lys	Leu	Glu	Ser	Gln	Met	Met	Ala	Met	Val	Glu	Arg				
785										790					795				
His	Glu	Thr	Gln	Val	Arg	Met	Leu	Lys	Gln	Arg	Ile	Ala	Leu	Leu	Glu				
805										810					815				
Glu	Glu	Asn	Ser	Arg	Pro	His	Thr	Asn	Glu	Thr	Ser	Leu							
820										825									

&lt;210&gt; 267

&lt;211&gt; 4181

&lt;212&gt; DNA

<213> Homo sapiens

<400> 267

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gaaatatgga aacgactcct cggccgagctc gagtgcagctc cattcagcag cccctggcctc 300  
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 cctcattctgg gactccaaca agaagataga cogyctgcga ggcaccacaag agtctaccat 540  
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 ctctcgaaatc atggaccaag accagacctc tgtctctatc cccgaaaacc agtctaccat 660  
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 ggaactgtga tttgttact acagcaaggg tttggtttcc aagtccggg tctcaacttt 3240  
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 acaggtgta ctacagctcc cagatacact aaagttaaca acagaccac accagagctg 3360  
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```

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cagagtggagg gaattggtagt taaggcttct tttttgcccc cagatcacatg gtgatgggta 3840
gcattatgggt cttataaagggt taaatttcaa gcaaaatgct tacaggggcta ggcagtagca 3900
aagtaactcga attattttcag gaagggtcttc aatcttaaaa caaattccatt attctttttc 3960
agtttttacct ctctctctctc agttctacac tgatacactt gaaggaccat ttactgtttt 4020
tttctgtagc accagagaat ccatccaaag ttcctatga aaaatgtgtt ccattgccat 4080
agctgactac aaattaaagt tgaggagggt tctgcataga gtcttttatgt ccataagcta 4140
cggttaggtc tatttttcaga gcatgatata aattccacag g 4181

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<210> 268  
 <211> 1172  
 <212> DNA  
 <213> Homo sapiens

```

<400> 268
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ggacagtttt tccgcagcct ctccggccacc accctcgaca gtggcggggcg accgcatgtct 180
gtgatgtgggt ctggccctca gctacttacc cactactatg atgatgcccgc gaccatgtac 240
caggtgttccc gccgtgggct tagcatctca ggggaatgggc cctgtctctgg ttccaggaag 300
cctaagcagc cttaccagtg gctgtcctac caggaggttg ccgacagggc tgaattttctg 360
gggtccggac ttctccagca caattgtaaa gcactgcactg atcagtttat tgggtgttttt 420
gcacaaaatc ggcacagatg gatcatttgt gagctggcct gctacacata ttccatgggt 480
gtgtgtccgc tctatgacac cctgggccctt ggggctatcc gctacatcat caatacagcg 540
gacatcagca ccgtgattgt ggacaaacct cagaaggctg tgcttctgct agagcatgtg 600
gagaggaaagg agactccagg cctcaagctg atcatcctca tggacccatt cgaagaagcc 660
ctgaagagaga gagggcagaa gtgcgggggtg gtcatlaagt ccatgcaggc cgtggaggac 720
tgtggccaag agaatcacca ggctcctgtg ccccgccagc ctgatgacct ctccattgtg 780
tgttttcacaa gcggccagac agggaaacca aaagggtcga tgctcaccga tgggaaactgt 840
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gatgtgcaca ttctctattt gcttttagca cacatgtttg agcgaatggt gcagctgtctc 960
gtctattgcc accggaggcg tgttggcttc ttccagggag atatccgcct tctctcagat 1020
gacatgaggg cctatgccc caccatcttc cctgtggctc caccagctgt gaaccggatg 1080
tacgacaaga tcttcagcca ggcaaacaca ccattaaagc gctggctctc ggaagtgtgca 1140
gc aaagcgta agcaagccga gaagccgaat tc 1172

```

<210> 269  
 <211> 318  
 <212> PRT  
 <213> Homo sapiens

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<400> 269
Asn His Ile Met Val Ser Val Ser Pro Pro Glu Glu His Ala Met Pro
1 5 10 15

Ile Gly Arg Ile Ala Asp Val Gln His Ile Lys Arg Arg Asp Ile Val
20 25 30

Leu Lys Arg Glu Leu Gly Glu Gly Ala Phe Gly Lys Val Phe Leu Ala
35 40 45

Glu Cys Tyr Asn Leu Ser Pro Thr Lys Asp Lys Met Leu Val Ala Val
50 55 60

Lys Ala Leu Lys Asp Pro Thr Leu Ala Ala Arg Lys Asp Phe Gln Arg
65 70 75 80

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Glu	Ala	Glu	Leu	Leu	Thr	Asn	Leu	Gln	His	Glu	His	Ile	Val	Lys	Phe
			85						90					95	
Tyr	Gly	Val	Cys	Gly	Asp	Gly	Asp	Pro	Leu	Ile	Met	Val	Phe	Glu	Tyr
			100					105					110		
Met	Lys	His	Gly	Asp	Leu	Asn	Lys	Phe	Leu	Arg	Ala	His	Gly	Pro	Asp
			115				120					125			
Ala	Met	Ile	Leu	Val	Asp	Gly	Gln	Pro	Arg	Gln	Ala	Lys	Gly	Glu	Leu
			130				135					140			
Gly	Leu	Ser	Gln	Met	Leu	His	Ile	Ala	Ser	Gln	Ile	Ala	Ser	Gly	Met
145					150					155					160
Val	Tyr	Leu	Ala	Ser	Gln	His	Phe	Val	His	Arg	Asp	Leu	Ala	Thr	Arg
				165					170					175	
Asn	Cys	Leu	Val	Gly	Ala	Asn	Leu	Leu	Val	Lys	Ile	Gly	Asp	Phe	Gly
			180					185					190		
Met	Ser	Arg	Asp	Val	Tyr	Ser	Thr	Asp	Tyr	Tyr	Arg	Val	Gly	Gly	His
			195				200					205			
Thr	Met	Leu	Pro	Ile	Arg	Trp	Met	Pro	Pro	Glu	Ser	Ile	Met	Tyr	Arg
						215					220				
Lys	Phe	Thr	Thr	Glu	Ser	Asp	Val	Trp	Ser	Phe	Gly	Val	Ile	Leu	Trp
225					230					235					240
Glu	Ile	Phe	Thr	Tyr	Gly	Lys	Gln	Pro	Trp	Phe	Gln	Leu	Ser	Asn	Thr
				245					250					255	
Glu	Val	Ile	Glu	Cys	Ile	Thr	Gln	Gly	Arg	Val	Leu	Glu	Arg	Pro	Arg
			260					265					270		
Val	Cys	Pro	Lys	Glu	Val	Tyr	Asp	Val	Met	Leu	Gly	Cys	Trp	Gln	Arg
			275				280					285			
Glu	Pro	Gln	Gln	Arg	Leu	Asn	Ile	Lys	Glu	Ile	Tyr	Lys	Ile	Leu	His
						295					300				
Ala	Leu	Gly	Lys	Ala	Thr	Pro	Ile	Tyr	Leu	Asp	Ile	Leu	Gly		
305					310					315					

<210> 270

<211> 980

&lt;212&gt; DNA

<213> Homo sapiens

<400> 270

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gccttggaa	aggtcttca	ggccgagtg	tacaacctc	gccgcacaa	ggcacaagt	180
ctgtggcgt	tgaagcccat	gaagctacc	acctggctg	cccgagata	tttccagag	240
ctgtgcgac	tgatcaccac	ctctcaqcat	gcagacatc	tcaagttta	tttaagtgc	300



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```

ggcgatggggg accccctcat catggtcttt gaatacatga agcatggaga cctgaataag 360
ttcctcaggg cccatggggc agatgcaatg atccttgttg atggacagcc acgccaaggcc 420
aaggggtgagc tggggctctc ccaaatgctc cacattgcca gtcagatgcg ctccgggtatg 480
gtgtaccctgg cctcccagca ctttgtgcac cgagacctgg ccaccaggaa ctgcctgggt 540
ggagcgaatc tgctagtga gattggggac ttcggcatgt ccagagatgt ctacagcagc 600
gattattaca ggggtgggag acacaccatg ctccccattc gctggatgcc tctcgaagcg 660
atcatgtacc ggaagtccac tacagagagt gatgtatgga gcttcggggg gatcctctgg 720
gagatcttca cctatggaaa gcagccatgg ttccaaactc caaacacgga ggtcattgag 780
tgcatatccc aaggtcgtgt tttggagcgg ccccgagtct gccccaaga ggtgtacgat 840
gtcatctcgg ggtgcctggc gagggaaacca cagcagcggt tgaacatcaa ggagatctac 900
aaaatctccc atgctttggg gaaggccacc ccaatctacc tggacattct tggctagtgg 960
tggctgtgtg tcattgaattc                                     980

```

&lt;210&gt; 271

&lt;211&gt; 408

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 271

```

Glu Asn Asn His Gln Glu Ser Tyr Pro Leu Ser Val Ser Pro Met Glu
 1             5             10            15

Asn Asn His Cys Pro Ala Ser Ser Glu Ser His Pro Lys Pro Ser Ser
      20             25             30

Pro Arg Gln Glu Ser Thr Arg Val Ile Gln Leu Met Pro Ser Pro Ile
      35             40             45

Met His Pro Leu Ile Leu Asn Pro Arg His Ser Val Asp Phe Lys Gln
      50             55             60

Ser Arg Leu Ser Glu Asp Gly Leu His Arg Glu Gly Lys Pro Ile Asn
      65             70             75             80

Leu Ser His Arg Glu Asp Leu Ala Tyr Met Asn His Ile Met Val Ser
      85             90             95

Val Ser Pro Pro Glu Glu His Ala Met Pro Ile Gly Arg Ile Ala Asp
      100            105            110

Val Gln His Ile Lys Arg Arg Asp Ile Val Leu Lys Arg Glu Leu Gly
      115            120            125

Glu Gly Ala Phe Gly Lys Val Phe Leu Ala Glu Cys Tyr Asn Leu Ser
      130            135            140

Pro Thr Lys Asp Lys Met Leu Val Ala Val Lys Ala Leu Lys Asp Pro
      145            150            155            160

Thr Leu Ala Ala Arg Lys Asp Phe Gln Arg Glu Ala Glu Leu Leu Thr
      165            170            175

Asn Leu Gln His Glu His Ile Val Lys Phe Tyr Gly Val Cys Gly Asp
      180            185            190

Gly Asp Pro Leu Ile Met Val Phe Glu Tyr Met Lys His Gly Asp Leu
      195            200            205

```

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Asn Lys Phe Leu Arg Ala His Gly Pro Asp Ala Met Ile Leu Val Asp  
 210 215 220  
 Gly Gln Pro Arg Gln Ala Lys Gly Glu Leu Gly Leu Ser Gln Met Leu  
 225 230 235 240  
 His Ile Ala Ser Gln Ile Ala Ser Gly Met Val Tyr Leu Ala Ser Gln  
 245 250 255  
 His Phe Val His Arg Asp Ile Ala Thr Arg Asn Cys Leu Val Gly Ala  
 260 265 270  
 Asn Leu Leu Val Lys Ile Gly Asp Phe Gly Met Ser Arg Asp Val Tyr  
 275 280 285  
 Ser Thr Asp Tyr Tyr Arg Val Gly Gly His Thr Met Leu Pro Ile Arg  
 290 295 300  
 Trp Met Pro Pro Glu Ser Ile Met Tyr Arg Lys Phe Thr Thr Glu Ser  
 305 310 315 320  
 Asp Val Trp Ser Phe Gly Val Ile Leu Trp Glu Ile Phe Thr Tyr Gly  
 325 330 335  
 Lys Gln Pro Trp Phe Gln Leu Ser Asn Thr Glu Val Ile Glu Cys Ile  
 340 345 350  
 Thr Gln Gly Arg Val Leu Glu Arg Pro Arg Val Cys Pro Lys Glu Val  
 355 360 365  
 Tyr Asp Val Met Leu Gly Cys Trp Gln Arg Glu Pro Gln Gln Arg Leu  
 370 375 380  
 Asn Ile Lys Glu Ile Tyr Lys Ile Leu His Ala Leu Gly Lys Ala Thr  
 385 390 395 400  
 Pro Ile Tyr Leu Asp Ile Leu Gly  
 405

&lt;210&gt; 272

&lt;211&gt; 1403

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 272

gagaacaacc accaggagtc ctaccctctg tcaagtgtct ccatggagaa taatcaactgc 60  
 ccagcgtcct ccgagtccca cccgaagcca tccagccccc ggccaggagag cacacgcgtg 120  
 atccagctga tgcccagccc catcatgcaac cctctgatcc tgaaccccgc gcaatccgtg 180  
 gatttcaaac agtccaggct ctccaggagc gggctgcata gggaaggaa gccatcaaac 240  
 ctctctcatc ggggaagacct ggcttacatg aaccacatca tggctctctg ctccccgcct 300  
 gaagagcacg ccatgcccat tgggagaata gcagatgtgc agcacattaa gaggagagac 360  
 atcgtgctga agcgagaact ggggtgagga gcctttggaa aggtcttcct ggccgagtg 420  
 tacaacctca gcccgaccaa ggacaagatg cttgtggctg tgaagggcct gaaggatccc 480  
 accctggctg cccggaagga ttccagagg gaggccgagc tgctcaccaa cctgcagcat 540  
 gagcacattg tcaagtctta tggagtgtgc gggcatgggg accccctcat catggtcttt 600  
 gaatacatga agcatggaga cctgaataag ttccctcagg cccatgggcc agatgcaatg 660

220/299

```

atccttgtgg atggacagcc acgcccaggcc aaggggtgagc tgggggtctc ccaaatgtc 720
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cgagacctgg ccaccaggaa ctgectgggt ggagogaate tgctagttaa gattggggac 840
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ctcccatcct gctggatgcc tcttgaaagc atcatgtacc ggaagtccac tacagagagt 960
gatgtatgga gcttcggggg gatcctctgg gagatcttca cctatggaaa gcagccatgg 1020
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aaaaaaaaa aaaaaaaaaa aaa

```

&lt;210&gt; 273

&lt;211&gt; 536

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 273

```

Met Gly Ser Asn Lys Ser Lys Pro Lys Asp Ala Ser Gln Arg Arg Arg
  1             5             10             15

```

```

Ser Leu Glu Pro Ala Glu Asn Val His Gly Ala Gly Gly Gly Ala Phe
             20             25             30

```

```

Pro Ala Ser Gln Thr Pro Ser Lys Pro Ala Ser Ala Asp Gly His Arg
  35             40             45

```

```

Gly Pro Ser Ala Ala Phe Ala Pro Ala Ala Ala Glu Pro Lys Leu Phe
  50             55             60

```

```

Gly Gly Phe Asn Ser Ser Asp Thr Val Thr Ser Pro Gln Arg Ala Gly
  65             70             75             80

```

```

Pro Leu Ala Gly Gly Val Thr Thr Phe Val Ala Leu Tyr Asp Tyr Glu
  85             90             95

```

```

Ser Arg Thr Glu Thr Asp Leu Ser Phe Lys Lys Gly Glu Arg Leu Gln
  100            105            110

```

```

Ile Val Asn Asn Thr Glu Gly Asp Trp Trp Leu Ala His Ser Leu Ser
  115            120            125

```

```

Thr Gly Gln Thr Gly Tyr Ile Pro Ser Asn Tyr Val Ala Pro Ser Asp
  130            135            140

```

```

Ser Ile Gln Ala Glu Glu Trp Tyr Phe Gly Lys Ile Thr Arg Arg Glu
  145            150            155            160

```

```

Ser Glu Arg Leu Leu Leu Asn Ala Glu Asn Pro Arg Gly Thr Phe Leu
  165            170            175

```

```

Val Arg Glu Ser Glu Thr Thr Lys Gly Ala Tyr Cys Leu Ser Val Ser
  180            185            190

```

```

Asp Phe Asp Asn Ala Lys Gly Leu Asn Val Lys His Tyr Lys Ile Arg

```

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195	200	205
Lys Leu Asp Ser Gly Gly Phe Tyr Ile Thr Ser Arg Thr Gln Phe Asn 210	215	220
Ser Leu Gln Gln Leu Val Ala Tyr Tyr Ser Lys His Ala Asp Gly Leu 225	230	235
Cys His Arg Leu Thr Thr Val Cys Pro Thr Ser Lys Pro Gln Thr Gln 245	250	255
Gly Leu Ala Lys Asp Ala Trp Glu Ile Pro Arg Glu Ser Leu Arg Leu 260	265	270
Glu Val Lys Leu Gly Gln Gly Cys Phe Gly Glu Val Trp Met Gly Thr 275	280	285
Trp Asn Gly Thr Thr Arg Val Ala Ile Lys Thr Leu Lys Pro Gly Thr 290	295	300
Met Ser Pro Glu Ala Phe Leu Gln Glu Ala Gln Val Met Lys Lys Leu 305	310	315
Arg His Glu Lys Leu Val Gln Leu Tyr Ala Val Val Ser Glu Glu Pro 325	330	335
Ile Tyr Ile Val Thr Glu Tyr Met Ser Lys Gly Ser Leu Leu Asp Phe 340	345	350
Leu Lys Gly Glu Thr Gly Lys Tyr Leu Arg Leu Pro Gln Leu Val Asp 355	360	365
Met Ala Ala Gln Ile Ala Ser Gly Met Ala Tyr Val Glu Arg Met Asn 370	375	380
Tyr Val His Arg Asp Leu Arg Ala Ala Asn Ile Leu Val Gly Glu Asn 385	390	395
Leu Val Cys Lys Val Ala Asp Phe Gly Leu Ala Arg Leu Ile Glu Asp 405	410	415
Asn Glu Tyr Thr Ala Arg Gln Gly Ala Lys Phe Pro Ile Lys Trp Thr 420	425	430
Ala Pro Glu Ala Ala Leu Tyr Gly Arg Phe Thr Ile Lys Ser Asp Val 435	440	445
Trp Ser Phe Gly Ile Leu Leu Thr Glu Leu Thr Thr Lys Gly Arg Val 450	455	460
Pro Tyr Pro Gly Met Val Asn Arg Glu Val Leu Asp Gln Val Glu Arg 465	470	475
Gly Tyr Arg Met Pro Cys Pro Pro Glu Cys Pro Glu Ser Leu His Asp 485	490	495
Leu Met Cys Gln Cys Trp Arg Lys Glu Pro Glu Glu Arg Pro Thr Phe 500	505	510

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Glu Tyr Leu Gln Ala Phe Leu Glu Asp Tyr Phe Thr Ser Thr Glu Pro  
 515 520 525

Gln Tyr Gln Pro Gly Glu Asn Leu  
 530 535

<210> 274  
 <211> 1611  
 <212> DNA  
 <213> Homo sapiens

<400> 274  
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 ccagcctcgg ccgacggcca ccgcggcccc agcgcggcgt tcgcccccg gcgcgcgag 180  
 cccaagctgt tggaggctt caactcctcg gacacgctca cctccccga gagggcgagg 240  
 ccgctggcgc gtggagtgac cacctttgtg gccctctat actatgagtc tagggcggag 300  
 acagaccctgt ccttcaagaa aggcgagcgg cttccagattg tcaacaacac agaggggagac 360  
 tgggtggctgg ccactcgtc cagcacaggc cagacaggct acatccccag caactacgtg 420  
 gcgcctccg actccatcca ggctgaggag tggatatgtt gcaagatcac cagacgggag 480  
 tcagagcggg tactgtctaa tgcagagaa cccagagggga ccttccctgt gcgagaaagt 540  
 gagaccacga aaggtgccta ctgcctctca gtgtctgact tcgacaacgc caagggcctc 600  
 aacgtgaagc actacaagat ccgcaagctg gacagcggcg gcttctacat cacctccgcg 660  
 acccagttca acagcctgca gcagctgggt gcctactact ccaaacacgc cgatggcctg 720  
 tgcacgcgcc tcaccacggt gtgccccacg tccaagcgc agactcaggc cctggccaag 780  
 gatgcctggg agatccctcg ggagtcgctg cggctggagg tcaagctggg ccagggtcgc 840  
 tttggcgagg tgtggatggg gacctggaac ggtaccacca ggggtggccat caaaacctg 900  
 aagcctggca cgaatgtccc agaggccttc ctgcaggagg cccaggtcat gaagaagctg 960  
 aggcatgaga agctggtgca gttgtatgct gtggtttcag aggagcccat ttacatcgtc 1020  
 acggagtaca tgagcaaggg gagtttgctg gactttctca agggggagac agggcaatgc 1080  
 ctgcggctgc ctacagctgtt ggacatggct gctcagatcg cctcaggcat ggcgtacgtg 1140  
 gagcggatga actaogtcca ccgggacctt cgtgcagcca acatcctggt gggagagaac 1200  
 ctggtgtgca aagtggccga ctttgggctg gctcggctca ttgaagacaa tgagtcacag 1260  
 gcgcggcaag gtgccaatt ccccatcaag tggacggctc cagaagctgc cctctatgct 1320  
 cgcttaccac tcaagtogga cgtgtgtgcc ttccggatcc tgctgactga gctcaccaca 1380  
 aagggacggg tgccctacc tgggatgggt aacgcgagg tgctggacca ggtggagcgg 1440  
 ggctaccgga tgccctccc gccggagtgt cccagtcctc tgacgcacct catgtgccag 1500  
 tgcctggcga agggagctga ggagcggccc accttcagat acctgcaggc cttcctggag 1560  
 gactacttca cgtccaccga gccccagtag cagccggggg agaactctca g 1611

<210> 275  
 <211> 226  
 <212> PRT  
 <213> Homo sapiens

<400> 275  
 Met Tyr His Ala Ser Lys Leu Ser Ile Asp Glu Glu Val Tyr Phe Glu  
 1 5 10 15  
 Asn Leu Met Gln Leu Val Glu His Tyr Thr Ser Asp Ala Asp Gly Leu  
 20 25 30  
 Cys Thr Arg Leu Ile Lys Pro Lys Val Met Glu Gly Thr Val Ala Ala  
 35 40 45

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Gln Asp Glu Phe Tyr Arg Ser Gly Trp Ala Leu Asn Met Lys Glu Leu  
 50 55 60  
 Lys Leu Leu Gln Thr Ile Gly Lys Gly Glu Phe Gly Asp Val Met Leu  
 65 70 75 80  
 Gly Asp Tyr Arg Gly Asn Lys Val Ala Val Lys Cys Ile Lys Asn Asp  
 85 90 95  
 Ala Thr Ala Gln Ala Phe Leu Ala Glu Ala Ser Val Met Thr Gln Leu  
 100 105 110  
 Arg His Ser Asn Leu Val Gln Leu Leu Gly Val Ile Val Glu Glu Lys  
 115 120 125  
 Gly Gly Leu Tyr Ile Val Thr Glu Tyr Met Ala Lys Gly Ser Leu Val  
 130 135 140  
 Asp Tyr Leu Arg Ser Arg Gly Arg Ser Val Leu Gly Gly Asp Cys Leu  
 145 150 155 160  
 Leu Lys Phe Ser Leu Asp Val Cys Glu Ala Met Glu Tyr Leu Glu Gly  
 165 170 175  
 Asn Asn Phe Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Ser  
 180 185 190  
 Glu Asp Asn Val Ala Lys Val Ser Asp Phe Gly Leu Thr Lys Glu Ala  
 195 200 205  
 Ser Thr Pro Arg Thr Arg Ala Ser Cys Gln Ser Ser Gly Gln Pro Leu  
 210 215 220  
 Arg Pro  
 225

&lt;210&gt; 276

&lt;211&gt; 2442

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 276

tccccggcgag cccccggcag ccagcgcgac gttccaaaat cgaacctcag tggcggcgct 60  
 cggaagcgga actctgcgag ggccgcgcgc gctacattgt gctgcggctg actctagagg 120  
 ctccccctcc tccccccgac tccctccctc cccttcccc cgcttttctt cctctcgcga 180  
 ccggggcgct gegtccgtcc cctgcctct gctggcggt cctctctccc ctctccttgc 240  
 acccatacct cttgtacag caccctctgg gtatcctgc gccctctccc tccccctga 300  
 ccgcatggag cgtcccgag gccgctgatg ccgccgcgc gacggtggcc cggaccgcag 360  
 tgcccccaaga gagctctaata ggtaccaagt gacagggttg ctaacttgag actcggggag 420  
 ccaagagctc ctgagaagat gtcagcaata caggccgcct ggccatccgg tacagaatgt 480  
 attgccaagt acaacttcca cggcaactgcc gagcagacc tgcccttctg caaaggagac 540  
 gtgctcacca ttgtggcggt caccaaggac cccaactggt acaaaagccaa aaacaagggt 600  
 gggcgtgagc gcactatccc agccaactac gtccagaagc gggaggggcgt gaaggcgggt 660  
 accaaactca gccctatgcc gtgagttcca cggcaagatc acacggggagc aggtctgagc 720  
 gctctgtac ccgccggaga caggcctgtt cctgggtgcg gagagcacca actaccgccg 780  
 agactacacg ctgtgcgtga gctgcgacgg caaggtggag cactacgcga tcatgtacca 840  
 tgccagcaag ctcagcatcg acgaggaggt gtactttgag aacctcatgc agctggtgga 900

224/299

```

gcactacacc tcagacgcag atggactctg tacgcgcctc attaaaccaa aggtcatgga 960
gggcacagtg gggcccaggg atgagttcta ccgcagcggc tgggcccctga acatgaagga 1020
gctgaagctg ctgcagacca tcgggaaggg ggagttcgga gacgtgatgc tgggcgatta 1080
ccgaggggaa aaagtgcgag tcaagtgcac taagaacgac gccactgccc aggccttccc 1140
ggctgaagcc tcagtcatga cgcaactgcg gcatagcaac ctgggtgcagc tccctgggcgt 1200
gatcgtggag gagaaggggc ggctctacat cgtcactgag tacatggcca aggggagcct 1260
tgtggactac ctgcggtcta ggggtcggtc agtgcctggc ggagactgtc tccccaagtt 1320
ctcgtcagat gtctcgcagg ccatggaata cctggagggc aacaatttgc tgcctcgaga 1380
cctggctgccc cgcaatgtgc tgggtgtctga ggacaacgtg gccaaagtca gcgactttgg 1440
tctaccaaag gaggcgtcca caccaggagc accggccaagc tgccagtcac gtggacagcc 1500
cctgaggccc tgagagagaa gaaattctcc actaagtctg acgtgtggag ttccggaaatc 1560
cttctctggg aaatctactc ctttgggcga gtgccttacc caagaattcc cctgaaggac 1620
gtcgtccctc ggggtggagaa gggctacaag atggatgccc ccgacggctg cccgcgccga 1680
gtctatgaag tcataagaa ctgctggcac ctggacgccc ccacgcccgc ctcccttcta 1740
cagctccagag agcagcttga gcacatcaaa acccagcagc tgcacctgtg acggctggcc 1800
tcgcctctgg tcattggcct gtggggactg aacctggaag atcatggacc tgggtcccct 1860
gctcactggg cccagcctg aactgagccc cagcgggctg cggggccttt ttccctcgct 1920
ccagctctca cccctccggc ccgctctctc ttggacccac ctgtggggcc tggggacccc 1980
actgaggggc caggagagaa ggaggccacg gaggcggagg cagcgcacca ccaactcggg 2040
cttccctggc ctcccgcacc tcgccttctc agagttttat tcccttccct ttttgagatt 2100
tttttccgt gtgtttattt tttattattt ttcaagataa ggagaagaa agtaccacgc 2160
aaatgggcat ttacaagaa gtacgaatct tatttttccct gtccctgccg tgagggtggg 2220
ggggaccggg cccctctcta gggacccctc gccccagcct cattcccatc ctctgtccc 2280
atgctccgtg tctcctcggt cgcctcgtgt ttgcgcttga ccactgttga ctgtttgcac 2340
gcgcccaggg cacagctctg tcaggggcctt ggaattcgtg tgccgctgcc acccgccacc 2400
ccgccttggt agatggaatt gtaataaac accgcatgag ga 2442

```

&lt;210&gt; 277

&lt;211&gt; 1114

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 277

```

Met Ala Lys Ala Thr Ser Gly Ala Ala Gly Leu Arg Leu Leu Leu Leu
  1             5             10             15

```

```

Leu Leu Leu Pro Leu Leu Gly Lys Val Ala Leu Gly Leu Tyr Phe Ser
      20             25             30

```

```

Arg Asp Ala Tyr Trp Glu Lys Leu Tyr Val Asp Gln Ala Ala Gly Thr
      35             40             45

```

```

Pro Leu Leu Tyr Val His Ala Leu Arg Asp Ala Pro Glu Glu Val Pro
      50             55             60

```

```

Ser Phe Arg Leu Gly Gln His Leu Tyr Gly Thr Tyr Arg Thr Arg Leu
      65             70             75             80

```

```

His Glu Asn Asn Trp Ile Cys Ile Gln Glu Asp Thr Gly Leu Leu Tyr
      85             90             95

```

```

Leu Asn Arg Ser Leu Asp His Ser Ser Trp Glu Lys Leu Ser Val Arg
      100            105            110

```

```

Asn Arg Gly Phe Pro Leu Leu Thr Val Tyr Leu Lys Val Phe Leu Ser
      115            120            125

```

225/299

Pro Thr Ser Leu Arg Glu Gly Glu Cys Gln Trp Pro Gly Cys Ala Arg  
 130 135 140  
 Val Tyr Phe Ser Phe Phe Asn Thr Ser Phe Pro Ala Cys Ser Ser Leu  
 145 150 155 160  
 Lys Pro Arg Glu Leu Cys Phe Pro Glu Thr Arg Pro Ser Phe Arg Ile  
 165 170 175  
 Arg Glu Asn Arg Pro Pro Gly Thr Phe His Gln Phe Arg Leu Leu Pro  
 180 185 190  
 Val Gln Phe Leu Cys Pro Asn Ile Ser Val Ala Tyr Arg Leu Leu Glu  
 195 200 205  
 Gly Glu Gly Leu Pro Phe Arg Cys Ala Pro Asp Ser Leu Glu Val Ser  
 210 215 220  
 Thr Arg Trp Ala Leu Asp Arg Glu Gln Arg Glu Lys Tyr Glu Leu Val  
 225 230 235 240  
 Ala Val Cys Thr Val His Ala Gly Ala Arg Glu Glu Val Val Met Val  
 245 250 255  
 Pro Phe Pro Val Thr Val Tyr Asp Glu Asp Asp Ser Ala Pro Thr Phe  
 260 265 270  
 Pro Ala Gly Val Asp Thr Ala Ser Ala Val Val Glu Phe Lys Arg Lys  
 275 280 285  
 Glu Asp Thr Val Val Ala Thr Leu Arg Val Phe Asp Ala Asp Val Val  
 290 295 300  
 Pro Ala Ser Gly Glu Leu Val Arg Arg Tyr Thr Ser Thr Leu Leu Pro  
 305 310 315 320  
 Gly Asp Thr Trp Ala Gln Gln Thr Phe Arg Val Glu His Trp Pro Asn  
 325 330 335  
 Glu Thr Ser Val Gln Ala Asn Gly Ser Phe Val Arg Ala Thr Val His  
 340 345 350  
 Asp Tyr Arg Leu Val Leu Asn Arg Asn Leu Ser Ile Ser Glu Asn Arg  
 355 360 365  
 Thr Met Gln Leu Ala Val Leu Val Asn Asp Ser Asp Phe Gln Gly Pro  
 370 375 380  
 Gly Ala Gly Val Leu Leu Leu His Phe Asn Val Ser Val Leu Pro Val  
 385 390 395 400  
 Ser Leu His Leu Pro Ser Thr Tyr Ser Leu Ser Val Ser Arg Arg Ala  
 405 410 415  
 Arg Arg Phe Ala Gln Ile Gly Lys Val Cys Val Glu Asn Cys Gln Ala  
 420 425 430  
 Phe Ser Gly Ile Asn Val Gln Tyr Lys Leu His Ser Ser Gly Ala Asn



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435		440		445
Cys Ser Thr Leu Gly Val	Val Thr Ser Ala Glu Asp Thr Ser Gly Ile			
450	455	460		
Leu Phe Val Asn Asp Thr Lys Ala Leu Arg Arg Pro Lys Cys Ala Glu				
465	470	475		480
Leu His Tyr Met Val Val Ala Thr Asp Gln Gln Thr Ser Arg Gln Ala				
485	490			495
Gln Ala Gln Leu Leu Val Thr Val Glu Gly Ser Tyr Val Ala Glu Glu				
500	505			510
Ala Gly Cys Pro Leu Ser Cys Ala Val Ser Lys Arg Arg Leu Glu Cys				
515	520			525
Glu Glu Cys Gly Gly Leu Gly Ser Pro Thr Gly Arg Cys Glu Trp Arg				
530	535			540
Gln Gly Asp Gly Lys Gly Ile Thr Arg Asn Phe Ser Thr Cys Ser Pro				
545	550			555
Ser Thr Lys Thr Cys Pro Asp Gly His Cys Asp Val Val Glu Thr Gln				
565	570			575
Asp Ile Asn Ile Cys Pro Gln Asp Cys Leu Arg Gly Ser Ile Val Gly				
580	585			590
Gly His Glu Pro Gly Glu Pro Arg Gly Ile Lys Ala Gly Tyr Gly Thr				
595	600			605
Cys Asn Cys Phe Pro Glu Glu Glu Lys Cys Phe Cys Glu Pro Glu Asp				
610	615			620
Ile Gln Asp Pro Leu Cys Asp Glu Leu Cys Arg Thr Val Ile Ala Ala				
625	630			635
Ala Val Leu Phe Ser Phe Ile Val Ser Val Leu Leu Ser Ala Phe Cys				
645	650			655
Ile His Cys Tyr His Lys Phe Ala His Lys Pro Pro Ile Ser Ser Ala				
660	665			670
Glu Met Thr Phe Arg Arg Pro Ala Gln Ala Phe Pro Val Ser Tyr Ser				
675	680			685
Ser Ser Gly Ala Arg Arg Pro Ser Leu Asp Ser Met Glu Asn Gln Val				
690	695			700
Ser Val Asp Ala Phe Lys Ile Leu Glu Asp Pro Lys Trp Glu Phe Pro				
705	710			715
Arg Lys Asn Leu Val Leu Gly Lys Thr Leu Gly Glu Gly Glu Phe Gly				
725	730			735
Lys Val Val Lys Ala Thr Ala Phe His Leu Lys Gly Arg Ala Gly Tyr				
740	745			750

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Thr Thr Val Ala Val Lys Met Leu Lys Glu Asn Ala Ser Pro Ser Glu  
 755 760 765  
 Leu Arg Asp Leu Leu Ser Glu Phe Asn Val Leu Lys Gln Val Asn His  
 770 775 780  
 Pro His Val Ile Lys Leu Tyr Gly Ala Cys Ser Gln Asp Gly Pro Leu  
 785 790 795 800  
 Leu Leu Ile Val Glu Tyr Ala Lys Tyr Gly Ser Leu Arg Gly Phe Leu  
 805 810 815  
 Arg Glu Ser Arg Lys Val Gly Pro Gly Tyr Leu Gly Ser Gly Gly Ser  
 820 825 830  
 Arg Asn Ser Ser Ser Leu Asp His Pro Asp Glu Arg Ala Leu Thr Met  
 835 840 845  
 Gly Asp Leu Ile Ser Phe Ala Trp Gln Ile Ser Gln Gly Met Gln Tyr  
 850 855 860  
 Leu Ala Glu Met Lys Leu Val His Arg Asp Leu Ala Ala Arg Asn Ile  
 865 870 875 880  
 Leu Val Ala Glu Gly Arg Lys Met Lys Ile Ser Asp Phe Gly Leu Ser  
 885 890 895  
 Arg Asp Val Tyr Glu Glu Asp Ser Tyr Val Lys Arg Ser Gln Gly Arg  
 900 905 910  
 Ile Pro Val Lys Trp Met Ala Ile Glu Ser Leu Phe Asp His Ile Tyr  
 915 920 925  
 Thr Thr Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile  
 930 935 940  
 Val Thr Leu Gly Gly Asn Pro Tyr Pro Gly Ile Pro Pro Glu Arg Leu  
 945 950 955 960  
 Phe Asn Leu Leu Lys Thr Gly His Arg Met Glu Arg Pro Asp Asn Cys  
 965 970 975  
 Ser Glu Glu Met Tyr Arg Leu Met Leu Gln Cys Trp Lys Gln Glu Pro  
 980 985 990  
 Asp Lys Arg Pro Val Phe Ala Asp Ile Ser Lys Asp Leu Glu Lys Met  
 995 1000 1005  
 Met Val Lys Arg Arg Asp Tyr Leu Asp Leu Ala Ala Ser Thr Pro Ser  
 1010 1015 1020  
 Asp Ser Leu Ile Tyr Asp Asp Gly Leu Ser Glu Glu Glu Thr Pro Leu  
 1025 1030 1035 1040  
 Val Asp Cys Asn Asn Ala Pro Leu Pro Arg Ala Leu Pro Ser Thr Trp  
 1045 1050 1055

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Ile Glu Asn Lys Leu Tyr Gly Met Ser Asp Pro Asn Trp Pro Gly Glu  
1060 1065 1070

Ser Pro Val Pro Leu Thr Arg Ala Asp Gly Thr Asn Thr Gly Phe Pro  
1075 1080 1085

Arg Tyr Pro Asn Asp Ser Val Tyr Ala Asn Trp Met Leu Ser Pro Ser  
1090 1095 1100

Ala Ala Lys Leu Met Asp Thr Phe Asp Ser  
1105 1110

&lt;210&gt; 278

&lt;211&gt; 393

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 278

Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln  
1 5 10 15

Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu  
20 25 30

Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp  
35 40 45

Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro  
50 55 60

Arg Met Pro Glu Ala Ala Pro Pro Val Ala Pro Ala Pro Ala Thr Pro  
65 70 75 80

Thr Pro Ala Ala Pro Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser  
85 90 95

Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly  
100 105 110

Phe Leu His Ser Gly Thr Ala Lys Ser Val Thr Cys Thr Tyr Ser Pro  
115 120 125

Ala Leu Asn Lys Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln  
130 135 140

Leu Trp Val Asp Ser Thr Pro Pro Pro Gly Thr Arg Val Arg Ala Met  
145 150 155 160

Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys  
165 170 175

Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln  
180 185 190

His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp  
195 200 205

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Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu  
 210 215 220  
 Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser  
 225 230 235 240  
 Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr  
 245 250 255  
 Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val  
 260 265 270  
 Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn  
 275 280 285  
 Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr  
 290 295 300  
 Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys  
 305 310 315 320  
 Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu  
 325 330 335  
 Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp  
 340 345 350  
 Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His  
 355 360 365  
 Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met  
 370 375 380  
 Phe Lys Thr Glu Gly Pro Asp Ser Asp  
 385 390

&lt;210&gt; 279

&lt;211&gt; 1303

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 279

gtccaggagc aggtagctgc tgggctccgg ggacactttg cgttcgggct gggagcgtgc 60  
 ttccacgacg ggtgacacgc ttccctggat tggcagccag actgccttcc gggcactgc 120  
 catggaggag ccgcagtcag atcctagcgt cgagcccccct ctgagtcagg aaacattttc 180  
 agacctatgg aaactacttc ctgaaaacaa cgttctgtcc cccttgccgt cccaagcaat 240  
 ggatgatttg atcgtgtccc cggaacgata tgaacaatgg ttcactgaag acccaggtcc 300  
 agatgaagct ccagaaatgc cagaggctgc tccccccgtg gccctgtcac cagcgactcc 360  
 tacacccggg gccctgtcac cagccccctc ctggcccctg tcatcttctg tccttccca 420  
 gaaaacctac cagggcagct acggtttccg tctggggttc ttgcattctg ggacagccaa 480  
 gtctgtgact tgcacgtact cccctgcccc caacaagatg ttttgccaac tggccaagac 540  
 ctgcccctgt cagctgtggg ttgattccac acccccgcgc ggcacccgcg tccgcgccat 600  
 ggccatctac aagcagtcac agcacatgac ggaggttgtg aggcgctgcc cccaccatga 660  
 gcgtgtctca gatagcgatg gtctggcccc tcctcagcat cttatccgag tggaaagaaa 720  
 tttgcgtgtg gagtatattg atgacagaaa cacttttcga catagtgtgg ttgtgcccta 780  
 tgagccgcct gaggttggct ctgactgtac caccatccac tacaactaca tgtgtaacag 840  
 ttctgtcatg ggccgcatga accggaggcc catcctcacc atcatcacac tgggaagactc 900

230/299

```

cagtggttaat ctactgggac ggaacagctt tgaggtgcgt gtttgtgcct gtctctgggag 960
agaccgggcg acagaggaag agaatctccg caagaaaggg gagcctcacc acgagctgcc 1020
cccaggggagc actaagcgag cactgcccaa caacaccagc tctctctccc agccaaagaa 1080
gaaaccactg gatggagaat atttcacct tcagatccgt gggcgtgagc gcttcgagat 1140
gttcgagagc ctgaatgagg cottggaact caagatgcc caggctggga aggagccagg 1200
ggggagcagg gctcactcca gccacctgaa gtccaaaaag ggtcagtccta cctcccgcga 1260
taaaaaactc atgttcaaga cagaagggcc tgactcagac tga 1303

```

&lt;210&gt; 280

&lt;211&gt; 448

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 280

```

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
  1                      5                      10                      15

```

```

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
  20                      25                      30

```

```

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
  35                      40                      45

```

```

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
  50                      55                      60

```

```

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
  65                      70                      75                      80

```

```

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Thr Ser Pro Tyr Asn
  85                      90                      95

```

```

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
  100                      105                      110

```

```

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
  115                      120                      125

```

```

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
  130                      135                      140

```

```

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
  145                      150                      155                      160

```

```

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
  165                      170                      175

```

```

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
  180                      185                      190

```

```

Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
  195                      200                      205

```

```

Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
  210                      215                      220

```

```

Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro

```

231/299

225		230		235		240
Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val						
	245			250		255
Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser						
	260		265		270	
Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu						
	275		280		285	
Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg						
	290	295		300		
Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile						
305		310		315		320
Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys						
	325		330		335	
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys						
	340		345		350	
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly						
	355		360		365	
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu						
	370		375		380	
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln						
385		390		395		400
Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys						
	405		410		415	
Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser						
	420		425		430	
Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro						
	435		440		445	

&lt;210&gt; 281

&lt;211&gt; 2816

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 281

```

tcgttgatat caaagacagt tgaaggaaat gaattttgaa acttcacggt gtgccacctt 60
acagtactgc cctgaccttt acatccagcg ttctgtagaa acccagctca ttctctcttg 120
aaagaaagtt attaccgac caccatgtcc cagagcacac agacaaatga attcctcagt 180
ccagagggtt tccagcatat ctgggatttt ctgggaacagc ctatatgttc agttcagccc 240
attgacttga actttgtgga tgaaccatca gaagatgggt cgacaaacaa gattgagatt 300
agcatggact gtatcgcgat gcaggactcg gacctgagtg acccctatgtg gccacagtac 360
acgaactctg ggcctctgaa cagcatggac cagcagattc agaacggctc ctgcgccacc 420
agtccttata acacagacca cgcgcagaa acgcgtcacgg cgccctcgcc ctacgcacag 480
cccagctcca ccttcgatgc tctctctcca tcaccgcga tcacctccaa caccgactac 540
ccaggcccg cagatttgcg cgtgtccttc cagcagtcga gcaccgcga gtcggccacc 600

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tggacgtatt ccaactgaact gaagaaactc tactgccaaa ttgcaaaagac atgccccatc 660
cagatacaagg tgatgaacccc acctctctcag ggagctgttta tccgcgccat gccctgtctac 720
aaaaaagctg agcagcgtcac ggaaggtgggt aagcgggtgcc ccaaccatga gctgcgcctg 780
gaattccaagc agggacacagat tgccccctctc agtcatattga ttccagtaga ggggaacacg 840
catgccacgt atgtagaaga tcccatcaca ggaagacaga gtgtgctggg acctatgag 900
ccaccaccag ttggcactga attcagcaga gtctgtgaca atttcatgtg taacagcagt 960
tgtgttggag ggatgaaccc cgttccaatt ttaatcattg ttaacttgga aaccagagat 1020
gggcaagctcc tgggcgcagc ctgcttttag gcccgagatc gtgcttgccc aggaagagac 1080
aggaaggcgg atgaagatag catcagaaag cagcaagttt cggacagatc aaagaacggg 1140
gatggtagca agcgcctcgt tcgtcagaa acacatggta tccagatgac atccatcaag 1200
aaacgaagat cccacagatga tgaactgtta tacttaccag tgaggggcgg tgagacttat 1260
gaaatgctgt tgaagatcaa agagtcctcg gaactcatgc agtaccttc ctagcacaca 1320
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gaogtctctt tttagacatt caagccccc aaccgatcag tgtaccata ggcctctatc 1500
tctatatctt aagtgtgtgt gttgtatttc catgtgtata tgtgagtgtg tgtgtgtgta 1560
tgtgtgtgct gtgtgatcta gccctcataa acaggacttg aagacacttt ggcctcagaa 1620
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gacccactgt gtttgtctgt gagcttctgt ttgtttctgt ggaggggagg gtcagggtgg 1800
gaaaggggca ttaagatggt tattggaacc cttttctgtc ttctctctgt gtctttctaa 1860
aatccacagg gaagcttttg agcaggtctc aaacttaaga tgtcttttta agaaaaggag 1920
aaaaaagttg ttattgtctg tgcataagta agttgtaggt gactgagaga ctgagtcaga 1980
cccttttaat gctggctcatg taataaattt gcaagtagta agaaacgaag gtgtcaagtg 2040
tactgtgggg cagcggaggtg atcattacca aaagtaatca actttgtggg ttgagagttc 2100
tttgtgagaa cttgcattat ttgtgtcttc cctcatgtgt taggtagaac atttctttaa 2160
gctgtgtacc tgccctctgc actgtatggt ggcctctgtt atgctaaagt tttctgttga 2220
catgaaaccc tggagagcct actacaaaaa aactgttgtt tggcccccac agcagggtgaa 2280
ctcattttgt gcttttaata gaaagacaaa tccaccccag taatattgoc ctacgtagt 2340
tgtttaocat tattcaaagc tcaaaataga atttgaagcc ctctcacaaa atctgtgatt 2400
aatttgctta attagagctt ctatccctca agcctacctc ccataaaacc agccatatta 2460
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caccagacct gattttctgt tcaccaagac aatgatttct gtgtattgag cctgtgtgct 2760
ttgtggatgt gtgattttaa ttttcaataa acttttgcac cttggtttaa aagaaa 2816

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&lt;210&gt; 282

&lt;211&gt; 641

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 282

```

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
1 5 10 15

```

```

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
20 25 30

```

```

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
35 40 45

```

```

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
50 55 60

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Ser Asp Pro Met Trp Phe Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser

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65	70	75	80
Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn	85	90	95
Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln	100	105	110
Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser	115	120	125
Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln	130	135	140
Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys	145	150	155
Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val	165	170	175
Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr	180	185	190
Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His	195	200	205
Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His	210	215	220
Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro	225	230	235
Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val	245	250	255
Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser	260	265	270
Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu	275	280	285
Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg	290	295	300
Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile	305	310	315
Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys	325	330	335
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys	340	345	350
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly	355	360	365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu	370	375	380



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Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400

Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser  
 405 410 415

Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser  
 420 425 430

Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg  
 435 440 445

Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile  
 450 455 460

Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu  
 465 470 475 480

Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser  
 485 490 495

His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly  
 500 505 510

Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr  
 515 520 525

Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp  
 530 535 540

Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys  
 545 550 555 560

Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His  
 565 570 575

Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser  
 580 585 590

Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg  
 595 600 605

Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe  
 610 615 620

Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly  
 625 630 635 640

Glu

&lt;210&gt; 283

&lt;211&gt; 2270

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 283

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tcgttgatata caaagacagt tgaaggaat gaattttgaa acttcacggt gtgccaccct 60
acagtaactgc cctgaccctt acatccagcg ttctgtagaa acccagctca tttctcttgg 120
aaagaaagttt attaccggtt caccatgtcc cagagcacac agacaaatga attcctcagt 180
ccagagggttt tccagcatat ctgggatttt ctggaacagc ctatatgttc agttcagccc 240
atctgacttga accttcttga tgaaacctca gaagatggtg cgacaaacaa agttgagatt 300
agcatggact gtatccgcat gcaggactcg gacctgagtg accccatgtg gccacagtac 360
acgaacctgg ggctcctgaa cagcatggac cagcagattc agaaccgctc ctggtccacc 420
agtcctctta acacagacca cgcgcagaac agcgtcacgg cgccctcgcc ctacgcacag 480
ccagctccca ccttcgatgc tctctctcca tcaccgccca tccctcccaa caccgatcac 540
ccaggcccgcc acagtttcga cgtgtctctc cagcagtcga gcaccgccaa gtccggccacc 600
tggaactgatt ccactgaact gaagaaatcc tactgccaaa ttgcaagac atgccccatc 660
cagatacaagg tgatgacccc acctcctcag ggagctgtta tccgcgccat gctgtctac 720
aaaaaagctg agcacgtcac ggagggtggtg aagcgtgtgc ccaaccatga gctgagccgt 780
gaattcaacg agggacagat tgcctctctc agtcatttga ttcgagtga ggtgaacagc 840
catgcccagt atgtagaaga tcccatcaca ggaagacaga gtgtgtgtgt accctatgag 900
ccaccctagg ttggcactga attcaccgca gtctgttaca atttcatgtg taacagcagt 960
tgtgttggag ggatgaaccg ccgtccaatt ttaactattg ttactcttga aaccagagat 1020
gggcaactcc ttggccgacg ctgcttggag gcccggtatc gtgcttgccc aggaagagac 1080
aggaaggcgg atgaagatag catcagaaga cagcaagttt cggacagtac aaagaacggt 1140
catggttaaga agcgcctggt tctcagaac acacatggtt tccagatgta atcoataag 1200
aaacgaagat cccacatga tgaactgtta tacttaccag tgaggggccc tgagacttat 1260
gaatgtctgt tgaagatcaa agagtccctg gaactcatgc agtaccttcc tcagcaacaa 1320
attgaactgt acaggcaaca gcaaccagcg cagcaccagc acttacttca gaacacagac 1380
tcaatcacagt tccactcttc atatggtaac agctccccc ctctgaacaa aatccacagc 1440
atgaacaacg tgcctcttgt gagccagctt atcaacctc agcagcgcaa cgccctcact 1500
cctacaacca ttccctgttg catggggacc aacattccca tgatggggac ccacatgcaa 1560
atggcttgag acatgaatgg actcagcccc acccaggcac tccctccccc actctccatg 1620
ccatccacct cccactgcac acccccacct cgtatccaa cagattgcag cattgtcggt 1680
ttcttagcga ggttgggctg ttcatcatgt ctggactatt tcaagaccca ggggctgac 1740
accatctatc agattggaga ttactccatg gatgatctgg caagcttgaa aatccctgag 1800
caattctgac atgggatctg gaaggggacc ctggaccacc ggcagctcca cgaattctcc 1860
tcccctttct atctctcgcg gaccccaagc agtgctctta cagtcagtgt gggctccagt 1920
gagaccgggg gtgagcgtgt tattgatgct gtgcatcca cctcgcgca gaccatctct 1980
ttcccaaccc gagatgagt gaatgacttc aactttgaca tggatgctcg ccgcaataag 2040
caacacgcga tcaaagagga gggggagtga gctcaccat gtgagctctt cctatcctct 2100
tcttaactcg cagcccctca aaagcactcc tgcttaatct tcaagccctt ctccctagct 2160
cctccccctt cctctgtctg atttcttagg ggaaggagaa gtaaggagct acctettacc 2220
taacatctga cctggcatct aattctgatt ctggctttaa gccttcaaaa 2270

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&lt;210&gt; 284

&lt;211&gt; 471

&lt;212&gt; FRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 284

```

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
1           5           10          15

```

```

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
20           25           30

```

```

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
35           40           45

```

```

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
50           55           60

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Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
 65 70 75 80  
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
 85 90 95  
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
 100 105 110  
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
 115 120 125  
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
 130 135 140  
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335  
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
 355 360 365  
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu

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370 375 380

Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400

Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser  
 405 410 415

Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser  
 420 425 430

Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg  
 435 440 445

Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Arg  
 450 455 460

Ser Gly Lys Ser Glu Asn Pro  
 465 470

&lt;210&gt; 285

&lt;211&gt; 2031

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 285

tgcgttgatat caaagacagt tgaaggaaat gaattttgaa acttcacggt gtgccaccct 60  
 acagtactgc cctgaccctt acatccagcg ttctgtagaa acccagctca ttctcttgg 120  
 aaagaagagtt attaccgatc caccatgtcc cagagcacac agacaaatga attctcagtt 180  
 ccagagggttt tccagcatat ctgggatttt ctggaacagc ctatatgttc agttcagccc 240  
 attgacttga actttgtgga tgaaccatca gaagatggtg cgacaaacaa gattgagatt 300  
 agcatggact gtatccgcat gcaggactcg gacctgagtg accccatgtg gccacagtac 360  
 acgaacctgg ggctcctgaa cagcatggac cagcagattc agaacggctc ctcgctccacc 420  
 agtccctata acacagacca cgccgacagg agcgtaacgg cgccctcgcc ctacgcacag 480  
 cccagctcca ccttcgatgc tctctctcca tcacccgcca tccctccaa caccgactac 540  
 ccaggcccg cactgttcga cgtgtccttc cagcagtcga gcaccgcca gtcggccacc 600  
 tggacgtatt ccactgaact gaagaaactc tactgcaaaa ttgcaaaagac atgccccatc 660  
 cagatcaagg tgatgacccc acctcctcag ggagctgtta tcgcgcgat cctgtgtctac 720  
 aaaaagacct agcacgtcac ggaggtggtg aagcggtgcc ccaaccatga gctgagccgt 780  
 gaattcaacg agggacagat tgcctcctcct agtcatttga ttcgagtaga ggggaacagc 840  
 catgcccagt atgtagaaga tcccatcaca ggaagacaga gtgtgctgtg acctattgag 900  
 ccacccacgg ttggcactga attcacgaca gtcttgata atttcattgt taacacagat 960  
 tgtgttgag ggatgaacgc cctccaattt ttaactcatt ttactctgga aaccagagat 1020  
 gggcagctcc tgggcccagc ctgctttgag gcccgagatc gtgcttgccc aggaagagac 1080  
 aggaagccgg atgaagatag catcagaagg cagcaagttt cggacagtat aaagaacggt 1140  
 gatggtacga agcgccgctt tcgtcagaac acacatggtta tccagatgac atccatcaag 1200  
 aaacgaagat cccagatga tgaactgtta tacttaccag tgagggggcg tgagacttat 1260  
 gaaatgctgt tgaagatcaa agagtccctg gaactcatgc agtaccttcc tcagcacaca 1320  
 attgaacagt acgggcaaca gcaacagcag cagcaccagc acttaacttca gaacagacc 1380  
 tcaatacagt ctccatttcc atattgttaac agctccccc ctctgaacaa acgtacagc 1440  
 atgaacaacg tgccttctgt gagccagctt atcaaccctc agcagcgcaa cgcctcact 1500  
 cctacaacca ttctctgagg catgggagcc aacagatctg gcaagtctga aaatccctga 1560  
 gcaatttcca catgcatctc ggaaggcat cctggaccac cggcagctcc acgaattctc 1620  
 ctccctcttc catctcctgc ggacccaag cagtgcctct acagtcaagt tgggctccag 1680  
 tgagaaacgg ggtgagcgtg ttattgatgc tgtgcgattc accctccgcc agacatctc 1740  
 ttctccacc ccagatgagt ggaatgactt caacttgac atggatgctc gccgcaataa 1800  
 gcaacagcgc atcaagagg agggggagtg agcctcacca tgtgagctct tccattcact 1860

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ctcctaactg ccagcccccct aaaagcactc ctgcttaatc ttcaaaagcct tctccctagc 1920  
 tctctccctt cctcttgctt gatttcttag gggaaggaga agtaaggagg taccctttac 1980  
 ctaacatctg acctggcatc taattctgat tctggcttta agccttcaaa a 2031

&lt;210&gt; 286

&lt;211&gt; 416

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 286

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
 1 5 10 15

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
 20 25 30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
 35 40 45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
 50 55 60

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65 70 75 80

His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
 85 90 95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
 100 105 110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Gln Gly  
 115 120 125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
 130 135 140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
 145 150 155 160

Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn  
 165 170 175

Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
 180 185 190

Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
 195 200 205

Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
 210 215 220

Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
 225 230 235 240

Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg  
 245 250 255

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Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
260 265 270

Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
275 280 285

His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
290 295 300

Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
305 310 315 320

Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
325 330 335

Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu  
340 345 350

Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser  
355 360 365

Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
370 375 380

Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
385 390 395 400

Ile Pro Asp Gly Met Gly Ala Asn Arg Ser Gly Lys Ser Glu Asn Pro  
405 410 415

&lt;210&gt; 287

<400> 287  
000

&lt;210&gt; 288

&lt;211&gt; 461

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 288

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
1 5 10 15

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
20 25 30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
35 40 45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
50 55 60

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
65 70 75 80

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His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
 85 90 95  
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
 100 105 110  
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
 115 120 125  
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
 130 135 140  
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
 145 150 155 160  
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn  
 165 170 175  
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
 180 185 190  
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
 195 200 205  
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
 210 215 220  
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
 225 230 235 240  
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg  
 245 250 255  
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
 260 265 270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
 275 280 285  
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
 290 295 300  
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
 325 330 335  
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu  
 340 345 350  
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser  
 355 360 365  
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
 370 375 380

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Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
 385 390 395 400

Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met  
 405 410 415

Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro  
 420 425 430

Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro  
 435 440 445

Tyr Pro Thr Asp Cys Ser Ile Val Gly Ile Trp Gln Val  
 450 455 460

&lt;210&gt; 289

<400> 289  
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<210> 290  
 <211> 586  
 <212> PRT  
 <213> Homo sapiens

<400> 290  
 Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
 1 5 10 15

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
 20 25 30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
 35 40 45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
 50 55 60

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65 70 75 80

His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
 85 90 95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
 100 105 110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
 115 120 125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
 130 135 140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
 145 150 155 160



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Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn  
 165 170  
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
 180 185 190  
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
 195 200 205  
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
 210 215 220  
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
 225 230 235 240  
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg  
 245 250 255  
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
 260 265 270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
 275 280 285  
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
 290 295 300  
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
 325 330 335  
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu  
 340 345 350  
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Tyr Gly Asn Ser  
 355 360 365  
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
 370 375 380  
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
 385 390 395 400  
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met  
 405 410 415  
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro  
 420 425 430  
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro  
 435 440 445  
 Tyr Pro Thr Asp Cys Ser Ile Val Gly Phe Leu Ala Arg Leu Gly Cys  
 450 455 460  
 Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr

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465					470					475					480
Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro															
				485					490					495	
Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln															
			500						505					510	
Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser															
			515						520					525	
Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val															
			530						535					540	
Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro															
			545											555	560
Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn															
				565										575	
Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu															
			580						585						

&lt;210&gt; 291

<400> 291  
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&lt;210&gt; 292

&lt;211&gt; 393

<212> PRT

<213> Homo sapiens

&lt;400&gt; 292

Met	Leu	Tyr	Leu	Glu	Asn	Asn	Ala	Gln	Thr	Gln	Phe	Ser	Glu	Pro	Gln
1				5					10					15	
Tyr	Thr	Asn	Leu	Gly	Leu	Leu	Asn	Ser	Met	Asp	Gln	Gln	Ile	Gln	Asn
			20					25					30		
Gly	Ser	Ser	Ser	Thr	Ser	Pro	Tyr	Asn	Thr	Asp	His	Ala	Gln	Asn	Ser
		35					40					45			
Val	Thr	Ala	Pro	Ser	Pro	Tyr	Ala	Gln	Pro	Ser	Ser	Thr	Phe	Asp	Ala
	50					55					60				
Leu	Ser	Pro	Ser	Pro	Ala	Ile	Pro	Ser	Asn	Thr	Asp	Tyr	Pro	Gly	Pro
65					70					75					80
His	Ser	Phe	Asp	Val	Ser	Phe	Gln	Gln	Ser	Ser	Thr	Ala	Lys	Ser	Ala
				85					90					95	
Thr	Trp	Thr	Tyr	Ser	Thr	Glu	Leu	Lys	Lys	Leu	Tyr	Cys	Gln	Ile	Ala
			100					105					110		
Lys	Thr	Cys	Pro	Ile	Gln	Ile	Lys	Val	Met	Thr	Pro	Pro	Pro	Gln	Gly

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115		120		125
Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr				
130		135		140
Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn				
145		150		160
Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn				
	165		170	175
Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val				
	180		185	190
Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val				
	195		200	205
Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg				
	210		215	220
Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val				
	225		230	235
Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg				
	245		250	255
Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp				
	260		265	270
Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr				
	275		280	285
His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp				
	290		295	300
Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu				
	305		310	315
Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His				
	325		330	335
Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu				
	340		345	350
Leu Gln Lys His Leu Leu Ser Ala Cys Phe Arg Asn Glu Leu Val Glu				
	355		360	365
Pro Arg Arg Glu Thr Pro Lys Gln Ser Asp Val Phe Phe Arg His Ser				
	370		375	380
Lys Pro Pro Asn Arg Ser Val Tyr Pro				
	385		390	

&lt;210&gt; 293

&lt;400&gt; 293

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245/299

&lt;210&gt; 294

&lt;211&gt; 471

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 294

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe  
 1 5 10 15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro  
 20 25 30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn  
 35 40 45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu  
 50 55 60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
 65 70 75 80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Thr Ser Pro Tyr Asn  
 85 90 95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
 100 105 110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
 115 120 125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
 130 135 140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175

Met Thr Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190

Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205

Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220

Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240

Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255

Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270

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Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335  
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
 355 360 365  
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu  
 370 375 380  
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400  
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser  
 405 410 415  
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser  
 420 425 430  
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg  
 435 440 445  
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Arg  
 450 455 460  
 Ser Gly Lys Ser Glu Asn Pro  
 465 470

&lt;210&gt; 295

&lt;400&gt; 295

000

&lt;210&gt; 296

&lt;211&gt; 516

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 296

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe  
 1 5 10 15  
 Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro  
 20 25 30

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Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn  
 35 40 45  
 Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu  
 50 55 60  
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
 65 70 75 80  
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
 85 90 95  
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
 100 105 110  
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
 115 120 125  
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
 130 135 140  
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335

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Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
 355 360 365  
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu  
 370 375 380  
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400  
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser  
 405 410 415  
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser  
 420 425 430  
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg  
 435 440 445  
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile  
 450 455 460  
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu  
 465 470 475 480  
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser  
 485 490 495  
 His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly  
 500 505 510  
 Ile Trp Gln Val  
 515

&lt;210&gt; 297

 <400> 297  
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&lt;210&gt; 298

&lt;211&gt; 641

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 298

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe  
 1 5 10 15  
 Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro  
 20 25 30  
 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn  
 35 40 45

249/299

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu  
 50 55 60  
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
 65 70 75 80  
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
 85 90 95  
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
 100 105 110  
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
 115 120 125  
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
 130 135 140  
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
 145 150 155 160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
 165 170 175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
 180 185 190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
 195 200 205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
 210 215 220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
 225 230 235 240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
 245 250 255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335  
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly



250/299

355	360	365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu		
370	375	380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln		
385	390	395
Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser		
405	410	415
Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser		
420	425	430
Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg		
435	440	445
Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile		
450	455	460
Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu		
465	470	475
Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser		
485	490	495
His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly		
500	505	510
Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr		
515	520	525
Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp		
530	535	540
Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys		
545	550	555
Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His		
565	570	575
Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser		
580	585	590
Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg		
595	600	605
Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe		
610	615	620
Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly		
625	630	635
640		

Glu

&lt;210&gt; 299

251/299

<400> 299  
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<210> 300  
<211> 448  
<212> FRT  
<213> Homo sapiens

<400> 300

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Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 1              5              10              15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
      20              25              30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
      35              40              45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
      50              55              60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
      65              70              75              80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Thr Ser Pro Tyr Asn
      85              90              95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
      100             105             110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
      115             120             125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
      130             135             140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
      145             150             155             160

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
      165             170             175

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
      180             185             190

Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
      195             200             205

Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
      210             215             220

Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
      225             230             235             240

Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
      245             250             255

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Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
 260 265 270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Val Thr Leu  
 275 280 285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
 290 295 300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335  
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
 355 360 365  
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu  
 370 375 380  
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400  
 Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys  
 405 410 415  
 Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser  
 420 425 430  
 Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro  
 435 440 445

&lt;210&gt; 301

 <400> 301  
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&lt;210&gt; 302

&lt;211&gt; 461

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 302

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
 1 5 10 15  
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
 20 25 30  
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
 35 40 45

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Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Thr Phe Asp Ala  
 50 55 60  
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65 70 75 80  
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
 85 90 95  
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
 100 105 110  
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
 115 120 125  
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
 130 135 140  
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
 145 150 155 160  
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn  
 165 170 175  
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
 180 185 190  
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
 195 200 205  
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
 210 215 220  
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
 225 230 235 240  
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg  
 245 250 255  
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
 260 265 270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
 275 280 285  
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
 290 295 300  
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
 325 330 335  
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu  
 340 345 350  
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser

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355                      360                      365  
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
 370                      375                      380  
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
 385                      390                      395                      400  
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met  
 405                      410                      415  
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro  
 420                      425                      430  
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro  
 435                      440                      445  
 Tyr Pro Thr Asp Cys Ser Ile Val Arg Ile Trp Gln Val  
 450                      455                      460

<210> 303  
 <211> 1386  
 <212> DNA  
 <213> Homo sapiens

<400> 303  
 atgttgtacc tggaaaaaaa tgcccagact caatttagtg agccacagta cagcaacctg 60  
 gggctctcga acagcatgga ccagcagatt cagaacggct cctcgtccac cagtcctcat 120  
 aacacagacc acgcgcagaa cagcgtcacg gcgcctcgc cctacgcaca gccacgctcc 180  
 accttcgatg ctctctctcc atcacccgcc atccctccca acaccgacta cccaggcccg 240  
 cacagtttgc acgtgtcctt ccagcagtcg agcaccccca agtcggccac ctggacgcat 300  
 tccactgaac tgaagaacct ctactgccaa attgcaaaaga catgccccat ccagatcaag 360  
 gtgatgacc caccctctca gggagctgtt atccgcgcca tgccgtgtca caaaaagct 420  
 gagcacgtca cggaggtggt gaagcggtcg cccaaccatg agctgagcgc tgaattcaac 480  
 gagggacaga ttgccctccc tagtcatttg attcgagtag aggggaacag ccatgcccg 540  
 tatgtagaag atcccatcac aggaagacag agtgtgctgg taccttatga gccaccccg 600  
 gttggcactg aattcacgac agtctgttac aatttcattg gtaacagcag ttgtgttgg 660  
 gggatgaacc gccgtccaat ttaatacatt gttactctgg aaaccagaga tgggcaagtc 720  
 ctgggcccag gctgcttga gcccgcgata tgtgcttgcc caggaagaga caggaaggcg 780  
 gatgaagata gcatcagaaa gcagcaagtt tcggacagta caaagaacgg tgatggtagc 840  
 aagcccccgt ttgcgcagaa cacacatggt atccagatga catccatcaa gaacagga 900  
 tcccagatg atgaactgtt atacttaccg gtgagggggc gtgagactta tgaatgctg 960  
 ttgaagatca aagagtcctt ggaactcatg cagtaccttc ctacgacac aattgaaag 1020  
 tacaggcaac agcaacagca ccagcaccag cacttacttc agaaacagac ctcaatacag 1080  
 tctccatctt catatggtaa cagctcccca cctctgaaca aaatgaacag catgaacaag 1140  
 ctgcctcttg tgagccagct tatcaacctt cagcagcgca acgcctcacc tctcaaac 1200  
 attcctgatg gcatgggagc caacattccc atgatgggga cccacatgcc aatggctgga 1260  
 gacatgaatg gactcagccc caccaggcca ctccctcccc cactctccat gccatccacc 1320  
 tcccactgca cacccccacc tccgtatccc acagattgca gcattgtcag gatctggcaa 1380  
 gctgta 1386

<210> 304  
 <211> 393  
 <212> PRT  
 <213> Homo sapiens

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&lt;400&gt; 304

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Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
 1              5              10              15

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
      20              25              30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35              40              45

Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50              55              60

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65              70              75              80

His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
      85              90              95

Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100              105              110

Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
 115              120              125

Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130              135              140

Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
 145              150              155              160

Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
      165              170              175

Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180              185              190

Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195              200              205

Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210              215              220

Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225              230              235              240

Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
      245              250              255

Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260              265              270

Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr
 275              280              285

His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290              295              300

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Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
305 310 315 320

Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
325 330 335

Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu  
340 345 350

Leu Gln Lys His Leu Leu Ser Ala Cys Phe Arg Asn Glu Leu Val Glu  
355 360 365

Pro Arg Arg Glu Thr Pro Lys Gln Ser Asp Val Phe Phe Arg His Ser  
370 375 380

Lys Pro Pro Asn Arg Ser Val Tyr Pro  
385 390

&lt;210&gt; 305

&lt;211&gt; 1182

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 305

atgttgtacc tggaaacaa tgcccagact caatttagtg agccacagta cacgaacctg 60  
gggtctctga acagcatgga ccagcagatt cagaacggct cctegtccac cagtccttat 120  
aacacagacc acgcgcagaa cagcgtcacg gcgcctctgc cctacgcaca gccacagctcc 180  
acctctgatg cctctctctc atcaccgcc atccctcca acaccgacta ccaggcccg 240  
cacagtttg acgtgtcctt ccagcagtcg agcaccgcc agtcggccac ctggacgtat 300  
tccactgaac tgaagaacct ctactgccaa attgcaaaga catgccccat ccagatcaag 360  
gtgatgacc caccctctca gggagctgtt atccgcgcca tgcctgtcta caaaaaagct 420  
gagcacgtca cggaggtggt gaagcgtgc cccaaccatg agctgagcgc tgaattcaac 480  
gagggacaga ttgccctcc tagtcatttg attcgagtag aggggaacag ccatgccccg 540  
tatgtagaag atcccctcac aggaagacag agtgtgtctg taccttatga gccacccccg 600  
gttggcactg aattcacgac agttctgtac aatttcattgt gtaacagcag ttgtgttgga 660  
gggtagaacc gcgcgtcaat tttatcatt gttaactctg aaaccagaga tgggcaagtc 720  
ctgggcgacg gctgcttga ggcgcggatc tgtgcttgcc caggaagaga caggaaggcg 780  
gatgaagata gcatcagaaa gcagcaagtt tcggacagta caaagaacgg tgatggtacg 840  
aagcgccctg ttogtcagaa cacacatggt atccagatga catccatcaa gaaacgaaga 900  
tcccagatg atgaactggt atacttacca gtgaggggccc gtgagactta tgaatgctg 960  
ttgaagatca aagagtcctt ggaactcatg cagtaccttc ctacgacac aattgaaacg 1020  
tacaggcaac agcaacagca gcagcaccag cacttacttc agaaacatct cctttcagcg 1080  
tgcttcagga atgagcttgt ggagccccgg agagaaatc caaaacaatc tgacgtcttc 1140  
tttagacatt ccaagccccc aaaccgatca gtgtaccat ag 1182

&lt;210&gt; 306

&lt;211&gt; 596

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 306

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln  
1 5 10 15

Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn  
20 25 30

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Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser  
 35 40 45  
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala  
 50 55 60  
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro  
 65 70 75 80  
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala  
 85 90 95  
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala  
 100 105 110  
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly  
 115 120 125  
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr  
 130 135 140  
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn  
 145 150 155 160  
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn  
 165 170 175  
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val  
 180 185 190  
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val  
 195 200 205  
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg  
 210 215 220  
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val  
 225 230 235 240  
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg  
 245 250 255  
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp  
 260 265 270  
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr  
 275 280 285  
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp  
 290 295 300  
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu  
 305 310 315 320  
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His  
 325 330 335



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Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln Gln His Gln His Leu  
 340 345 350  
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser  
 355 360 365  
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val  
 370 375 380  
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr  
 385 390 395 400  
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met  
 405 410 415  
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro  
 420 425 430  
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro  
 435 440 445  
 Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys  
 450 455 460  
 Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr  
 465 470 475 480  
 Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro  
 485 490 495  
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln  
 500 505 510  
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser  
 515 520 525  
 Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val  
 530 535 540  
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro  
 545 550 555 560  
 Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn  
 565 570 575  
 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu  
 580 585

&lt;210&gt; 307

&lt;211&gt; 1761

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 307

atgttgtagc tggaaaacaa tgcccagact caatttagtg agccacagta cagcaacctg 60  
 gggctcctga acagcatgga ccagcagatt cagaacggct cctcgtccac cagtccttat 120  
 aacacagacc acgcgcagaa cagcgtcagc gcgcctctgc cctacgcaca gccacagctcc 180

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accttctgatg ctctctctccc atcaccgccg atccccctcca acaccgacta cccaggcccg 240
cacagtcttcg acgtgtctctt ccagcagtcg agcaccccca agtcggccac ctggacgtat 300
tccactgtaac tgaagaaact ctactgccaa attgcaaaga catgccccat ccagatcaag 360
gtgatgaacc cactctctca gggagctgtt atcccgccca tgctgtctca caaaaaagct 420
gagcacgtca cggaggtggt gaagcgtgtg cccaaccatg agctgagcog tgaattcaac 480
ggggacacaga ttgccccctc tagtcatttg attcgagtag aggggaaacag ccatgccccag 540
tatgtagaag atccccctac aggaagacag agtgtgctgg taccttatga gccacccacg 600
gttggcactg aattcacgac agtcttgtac aatttcattg gtaacacgag ttgtgttgga 660
gggatgaacc gccgtccaat tttaatcatt gttactctgg aaaccagaga tgggcaagtc 720
ctgggcccagc gctgtcttga ggcccgagtc tgtgtctgcc caggaaagaga caggaaagtc 780
gatgaagata gcatcagaaa gcagcaagtt toggacagta caaagaacgg tgatgtgtac 840
aagcgccogt ttogtcagaa cacacatggt atccagatga catccatcaa gaaacagaga 900
tccccagatg atgaactgtt atacttacca gtgagggggc gtgagactta tgaatgctg 960
ttgaagatca aagagtccct ggaactcatg cagtaccttc ctgacacac aattgaaagc 1020
tacaggcaac agcaacacga gcagcacagg cacttacttc agaaacagac ctcaatacag 1080
tctccatctt catatggtta cagctcccca cctctgaaca aaatgaacag catgaacaag 1140
ctgcctcttg tgagccagct tatcaacctc cagcagcgca acgcccctac tctcaaaccc 1200
attcctgatg gcattgggagc caacattccc atgatgggca cccacatgcc aatggcttga 1260
gacatgaatg gactcagccc caccagggca ctccctcccc cactctccat gccatccacc 1320
tcccactgca cacccccacc tccgtatccc acagattgca gcattgtacg tttcttagcg 1380
aggttgggct gttcatcatg tctggactat ttcacgaccc aggggctgac caccatctat 1440
cagatttgagc attactccat ggaatgatcg gcaagtctga aaatccccga gaaatttcga 1500
catgagatctt ggaagggcat cctggaccac cggcagctcc acgaattctc ctccccctct 1560
catctctctg ggaacccaag cagtgcctct acagtcaagt tggggtccagc ttgagaccgg 1620
gggtgacgtg ttattgatgc tgtgcgattc accctccgac agaccattct ttccccacc 1680
cgagatgagt ggaatgactt caactttgac atggatgctc gccgcaataa gcaacagcgc 1740
atcaaagagg agggggagtg a

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&lt;210&gt; 308

&lt;211&gt; 516

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 308

```

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
1 5 10 15

```

```

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
20 25 30

```

```

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
35 40 45

```

```

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
50 55 60

```

```

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
65 70 75 80

```

```

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Thr Ser Pro Tyr Asn
85 90 95

```

```

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
100 105 110

```

```

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
115 120 125

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Asn Thr Asp Tyr Pro Gly	Pro His Ser Phe Asp Val Ser Phe Gln Gln
130	135 140
Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys	
145	150 155 160
Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val	
165	170
Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr	
180	185 190
Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His	
195	200 205
Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His	
210	215 220
Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro	
225	230 235 240
Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val	
245	250 255
Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser	
260	265 270
Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu	
275	280 285
Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg	
290	295 300
Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile	
305	310 315 320
Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys	
325	330 335
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys	
340	345 350
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly	
355	360 365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu	
370	375 380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln	
385	390 395 400
Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser	
405	410 415
Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser	
420	425 430

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Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg  
 435 440 445

Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile  
 450 455 460

Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu  
 465 470 475 480

Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser  
 485 490 495

His Cys Thr Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Arg  
 500 505 510

Ile Trp Gln Val  
 515

&lt;210&gt; 309

&lt;211&gt; 1551

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 309

atgtcccaga gcacacagac aaatgaattc ctacgtccag aggtttttcca gcatactctgg 60  
 gattttctctgg aacagccctat atgttccagtt cagcccatgt acttgaaact tbtggatgaa 120  
 ccattcagaag atggtgcgac aaacaagatt gagatttagca tggactgtat ccgcatgcag 180  
 gactcggacc ttagtgacc catgtggoca cagtacacga acctgggggt cctgaacagc 240  
 atggaccagc agattcagaa cggctcctcg tccaccagtc cctataaac agaccacgcy 300  
 cagaacagcg tcacggcgcc ctgcacctac gcacagccca gctccacct cgtatgctctc 360  
 tctccatcac ccgcatcccc ctccaacacc gactaccag gcccgcacag tttcgacgtg 420  
 tcttccagc agtcagcac cgccaagtgc gccacctgga cgtattccac tgaactgaag 480  
 aaactctact gccaaattgc aaagacatgc cccatccaga tcaaggtgat gacccacact 540  
 cctcagggag ctgttatccg cgccatgcct gtctacaaaa aagctgagca cgtcacggag 600  
 gtggtagaag ggtgcccaca ccatgagctg agccgtgaat tcaacgaggg acagattgcc 660  
 cctctagtc atttgattcg agtagagggg aacagccatg cccagttatg agaagatccc 720  
 atcacaggaa gacagagttg gctggtacct tatgagccac cccaggttgg cactgaattc 780  
 acgacagctc tgtacaattt catgtgtaac agcagttgtg ttggagggat gaaccgcgt 840  
 ccaattttta tcatgtttac tctggaaaac agagatgggc aagtcctggg ccgacgctgc 900  
 tttgagggccc ggaatctgtgc ttgcccagga agagacagga aggggatga agatagcatc 960  
 agaaagcagc aagtttcgga cagtacaaag aacggtgatg gtacgaagcg ccggtttctg 1020  
 cagaacacac atggtatcca gatgacatcc atcaagaaac gaagatcccc agatgatgaa 1080  
 ctgttatact taccagttag gggccgttag acttatgaaa tgcgtgtgaa gatcaagag 1140  
 tccctggaa ccatgcagta ccttctctag cacacaattg aaacgtacag gcaacagcaa 1200  
 cagcagcagc accagcactt acttcagaaa cagacctcaa tacagctctc atctctcat 1260  
 ggtaacagct ccccactctt gaacaaaatg aacagcatga acaagctggc tctgtgagc 1320  
 cagcttatca acctcagca gcgcaacgcc ctactcctca caaccattcc tgatggcatg 1380  
 ggagccaaca tctccatgat gggcaccacc atgccaatgg ctggagacat gaatggact 1440  
 agcaccaccc aggcactccc tcccactc tccatgccat ccactccca ctgcacaccc 1500  
 ccactcctgt atcccacaga ttgcagcatt gtcaggatct ggcaagctctg a 1551

&lt;210&gt; 310

&lt;211&gt; 641

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

262/299

&lt;400&gt; 310

```

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 1              5              10              15

Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
      20              25              30

Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
      35              40              45

Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
      50              55              60

Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
      65              70              75              80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
      85              90              95

Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
      100              105              110

Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
      115              120              125

Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
      130              135              140

Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
      145              150              155              160

Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
      165              170              175

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
      180              185              190

Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
      195              200              205

Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
      210              215              220

Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
      225              230              235              240

Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
      245              250              255

Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
      260              265              270

Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
      275              280              285

Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
      290              295              300

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Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
 305 310 315 320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys  
 325 330 335  
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys  
 340 345 350  
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly  
 355 360 365  
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu  
 370 375 380  
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln  
 385 390 395 400  
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser  
 405 410 415  
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser  
 420 425 430  
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg  
 435 440 445  
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile  
 450 455 460  
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu  
 465 470 475 480  
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser  
 485 490 495  
 His Cys Thr Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Ser  
 500 505 510  
 Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr  
 515 520 525  
 Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp  
 530 535 540  
 Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys  
 545 550 555 560  
 Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His  
 565 570 575  
 Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser  
 580 585 590  
 Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg  
 595 600 605  
 Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe

264/299

610

615

620

Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly  
 625 630 635 640

Glu

&lt;210&gt; 311

&lt;211&gt; 1926

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 311

atgtccacaga gcacacagac aaatgaattc ctacgtccag aggtttttcca gcatatctgg 60  
 gattttctgg aacagcctat atgttcagtt cagcccatg acttgaactt tgtggatgaa 120  
 ccacacagaag atgggtgcgac aaacaagatt gagattagca tggactgtat ccgcatgcag 180  
 gactcggacc tgagtgaacc catgtggcca cagtacacga acctggggct cctgaacagc 240  
 atggaccagc agattcagaa cggctcctgc tccaccagtc cctataacac agaccacgog 300  
 cagaacacagc tcaaggcgcc ctgcgcctac gcacagccca gctccacctt cgtgctcttc 360  
 tctccatcac ccgcatcccc ctccaacacc gactacccag gcccgacagc tttcgacgtg 420  
 tccttccagc agtcgagcac cgccaagtgc gccacctgga cgtattccac tgaactgaag 480  
 aaactctact gccaaattgc aaagacatgc cccatccaga tcaaggtgat gacccacctt 540  
 cctcagggag ctgttatccg cgccatgctt gtctacaaaa aagctgagca cgtcacggag 600  
 gtgggtgaagc ggtgccccaa ccatgagctg agccgtgaat tcaacgaggg acagattgcc 660  
 cctcctagtc atttgattcg agtagagggg aacagccatg cccagtatgt agaagatccc 720  
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 ccaattttaa tcattgttac tctggaaacc agagatgggc aagtcctggg ccgacgctgc 900  
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 cagaacacac atgggtatcca gatgacatcc atcaagaaac gaagatcccc agatgatgaa 1080  
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 cagcagcagc accagcactt acttcagaaa cagacctcaa tacagtcctc atcttcatat 1260  
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 ccactctcgt atccacagca tgcagcatt gtacgtttct tagcaggtt gggctgttca 1560  
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 gatgctgtgc gattcacctc ccgcagacc atctcttcc caccocgaga tgaatggaaat 1860  
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 gagtga 1926

&lt;210&gt; 312

&lt;211&gt; 448

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 312

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe  
 1 5 10 15

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Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro  
                   20                  25                  30  
 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn  
                   35                  40                  45  
 Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu  
                   50                  55                  60  
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser  
                   65                  70                  75                  80  
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn  
                   85                  90                  95  
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln  
                   100                  105                  110  
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser  
                   115                  120                  125  
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln  
                   130                  135                  140  
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys  
                   145                  150                  155                  160  
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val  
                   165                  170                  175  
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr  
                   180                  185                  190  
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His  
                   195                  200                  205  
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His  
                   210                  215                  220  
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro  
                   225                  230                  235                  240  
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val  
                   245                  250                  255  
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser  
                   260                  265                  270  
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu  
                   275                  280                  285  
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg  
                   290                  295                  300  
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile  
                   305                  310                  315                  320  
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys



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325	330	335
Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys		
340	345	350
Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly		
355	360	365
Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu		
370	375	380
Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln		
385	390	395
Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys		
405	410	415
Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser		
420	425	430
Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro		
435	440	445

<210> 313  
 <211> 2816  
 <212> DNA  
 <213> Homo sapiens

<400> 313  
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 tgtgtgtcgc tgtgtatcta gccctcataa acaggacttg aagacacttt ggctcagaga 1620  
 cccaactgct caaaggcaca aagccactag tgagagaatc ttttgaaggg actcaaacct 1680

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&lt;210&gt; 314

&lt;211&gt; 499

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 314

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Met Ala Gln Ser Thr Ala Thr Ser Pro Asp Gly Gly Thr Thr Phe Glu
  1             5             10             15

His Leu Trp Ser Ser Leu Glu Pro Asp Ser Thr Tyr Phe Asp Leu Pro
      20             25             30

Gln Ser Ser Arg Gly Asn Asn Glu Val Val Gly Gly Thr Asp Ser Ser
      35             40             45

Met Asp Val Phe His Leu Glu Gly Met Thr Thr Ser Val Met Ala Gln
  50             55             60

Phe Asn Leu Leu Ser Ser Thr Met Asp Gln Met Ser Ser Arg Ala Ala
  65             70             75             80

Ser Ala Ser Pro Tyr Thr Pro Glu His Ala Ala Ser Val Pro Thr His
      85             90             95

Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Thr Met Ser Pro Ala
      100             105             110

Pro Val Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His His Phe Glu
      115             120             125

Val Thr Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr
      130             135             140

Ser Pro Leu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro
      145             150             155             160

Ile Gln Ile Lys Val Ser Thr Pro Pro Pro Pro Gly Thr Ala Ile Arg

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165	170	175
Ala Met Pro Val Tyr Lys Lys	Ala Glu His Val Thr Asp Val Val Lys	
180	185	190
Arg Cys Pro Asn His Glu Leu Gly Arg Asp Phe Asn Glu Gly Gln Ser		
195	200	205
Ala Pro Ala Ser His Leu Ile Arg Val Glu Gly Asn Asn Leu Ser Gln		
210	215	220
Tyr Val Asp Asp Pro Val Thr Gly Arg Gln Ser Val Val Val Pro Tyr		
225	230	235
Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Ile Leu Tyr Asn Phe		
245	250	255
Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu		
260	265	270
Ile Ile Ile Thr Leu Glu Met Arg Asp Gly Gln Val Leu Gly Arg Arg		
275	280	285
Ser Phe Glu Gly Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala		
290	295	300
Asp Glu Asp His Tyr Arg Glu Gln Gln Ala Leu Asn Glu Ser Ser Ala		
305	310	315
Lys Asn Gly Ala Ala Ser Lys Arg Ala Phe Lys Gln Ser Pro Pro Ala		
325	330	335
Val Pro Ala Leu Gly Ala Gly Val Lys Lys Arg Arg His Gly Asp Glu		
340	345	350
Asp Thr Tyr Tyr Leu Gln Val Arg Gly Arg Glu Asn Phe Glu Ile Leu		
355	360	365
Met Lys Leu Lys Glu Ser Leu Glu Leu Met Glu Leu Val Pro Gln Pro		
370	375	380
Leu Val Asp Ser Tyr Arg Gln Gln Gln Gln Leu Leu Gln Arg Pro Ser		
385	390	395
His Leu Gln Pro Pro Ser Tyr Gly Pro Val Leu Ser Pro Met Asn Lys		
405	410	415
Val His Gly Gly Met Asn Lys Leu Pro Ser Val Asn Gln Leu Val Gly		
420	425	430
Gln Pro Pro Pro His Ser Ser Ala Ala Thr Pro Asn Leu Gly Pro Val		
435	440	445
Gly Pro Gly Met Leu Asn Asn His Gly His Ala Val Pro Ala Asn Gly		
450	455	460
Glu Met Ser Ser Ser His Ser Ala Gln Ser Met Val Ser Gly Ser His		
465	470	475
		480

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Cys Thr Pro Pro Pro Pro Tyr His Ala Asp Pro Ser Leu Val Arg Thr  
 485 490 495

Trp Gly Pro

<210> 315

<211> 636

<212> PRT

<213> Homo sapiens

<400> 315

Met Ala Gln Ser Thr Ala Thr Ser Pro Asp Gly Gly Thr Thr Phe Glu  
 1 5 10 15

His Leu Trp Ser Ser Leu Glu Pro Asp Ser Thr Tyr Phe Asp Leu Pro  
 20 25 30

Gln Ser Ser Arg Gly Asn Asn Glu Val Val Gly Gly Thr Asp Ser Ser  
 35 40 45

Met Asp Val Phe His Leu Glu Gly Met Thr Thr Ser Val Met Ala Gln  
 50 55 60

Phe Asn Leu Leu Ser Ser Thr Met Asp Gln Met Ser Ser Arg Ala Ala  
 65 70 75 80

Ser Ala Ser Pro Tyr Thr Pro Glu His Ala Ala Ser Val Pro Thr His  
 85 90 95

Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Thr Met Ser Pro Ala  
 100 105 110

Pro Val Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His His Phe Glu  
 115 120 125

Val Thr Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr  
 130 135 140

Ser Pro Leu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro  
 145 150 155 160

Ile Gln Ile Lys Val Ser Thr Pro Pro Pro Gly Thr Ala Ile Arg  
 165 170 175

Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr Asp Val Val Lys  
 180 185 190

Arg Cys Pro Asn His Glu Leu Gly Arg Asp Phe Asn Glu Gly Gln Ser  
 195 200 205

Ala Pro Ala Ser His Leu Ile Arg Val Glu Gly Asn Asn Leu Ser Gln  
 210 215 220

Tyr Val Asp Asp Pro Val Thr Gly Arg Gln Ser Val Val Val Pro Tyr  
 225 230 235 240

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Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Ile Leu Tyr Asn Phe  
 245 250 255  
 Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu  
 260 265 270  
 Ile Ile Ile Thr Leu Glu Met Arg Asp Gly Gln Val Leu Gly Arg Arg  
 275 280 285  
 Ser Phe Glu Gly Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala  
 290 295 300  
 Asp Glu Asp His Tyr Arg Glu Gln Gln Ala Leu Asn Glu Ser Ser Ala  
 305 310 315 320  
 Lys Asn Gly Ala Ala Ser Lys Arg Ala Phe Lys Gln Ser Pro Pro Ala  
 325 330 335  
 Val Pro Ala Leu Gly Ala Gly Val Lys Lys Arg Arg His Gly Asp Glu  
 340 345 350  
 Asp Thr Tyr Tyr Leu Gln Val Arg Gly Arg Glu Asn Phe Glu Ile Leu  
 355 360 365  
 Met Lys Leu Lys Glu Ser Leu Glu Leu Met Glu Leu Val Pro Gln Pro  
 370 375 380  
 Leu Val Asp Ser Tyr Arg Gln Gln Gln Gln Leu Gln Arg Pro Ser  
 385 390 395 400  
 His Leu Gln Pro Pro Ser Tyr Gly Pro Val Leu Ser Pro Met Asn Lys  
 405 410 415  
 Val His Gly Gly Met Asn Lys Leu Pro Ser Val Asn Gln Leu Val Gly  
 420 425 430  
 Gln Pro Pro Pro His Ser Ser Ala Ala Thr Pro Asn Leu Gly Pro Val  
 435 440 445  
 Gly Pro Gly Met Leu Asn Asn His Gly His Ala Val Pro Ala Asn Gly  
 450 455 460  
 Glu Met Ser Ser Ser His Ser Ala Gln Ser Met Val Ser Gly Ser His  
 465 470 475 480  
 Cys Thr Pro Pro Pro Pro Tyr His Ala Asp Pro Ser Leu Val Ser Phe  
 485 490 495  
 Leu Thr Gly Leu Gly Cys Pro Asn Cys Ile Glu Tyr Phe Thr Ser Gln  
 500 505 510  
 Gly Leu Gln Ser Ile Tyr His Leu Gln Asn Leu Thr Ile Glu Asp Leu  
 515 520 525  
 Gly Ala Leu Lys Ile Pro Glu Gln Tyr Arg Met Thr Ile Trp Arg Gly  
 530 535 540  
 Leu Gln Asp Leu Lys Gln Gly His Asp Tyr Ser Thr Ala Gln Gln Leu

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545                      550                      555                      560  
 Leu Arg Ser Ser Asn Ala Ala Thr Ile Ser Ile Gly Gly Ser Gly Glu  
                                  565                      570                      575  
 Leu Gln Arg Gln Arg Val Met Glu Ala Val His Phe Arg Val Arg His  
                                  580                      585                      590  
 Thr Ile Thr Ile Pro Asn Arg Gly Gly Pro Gly Gly Gly Pro Asp Glu  
                                  595                      600                      605  
 Trp Ala Asp Phe Gly Phe Asp Leu Pro Asp Cys Lys Ala Arg Lys Gln  
                                  610                      615                      620  
 Pro Ile Lys Glu Glu Phe Thr Glu Ala Glu Ile His  
                                  625                      630                      635

&lt;210&gt; 316

&lt;211&gt; 588

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 316

Met Asp Val Phe His Leu Glu Gly Met Thr Thr Ser Val Met Ala Gln  
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 Phe Asn Leu Leu Ser Ser Thr Met Asp Gln Met Ser Ser Arg Ala Ala  
                                   20                                  25                                  30  
 Ser Ala Ser Pro Tyr Thr Pro Glu His Ala Ala Ser Val Pro Thr His  
                                   35                                  40                                  45  
 Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Thr Met Ser Pro Ala  
                                   50                                  55                                  60  
 Pro Val Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His His Phe Glu  
   65                                  70                                  75                                  80  
 Val Thr Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr  
                                   85                                  90                                  95  
 Ser Pro Leu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro  
                                   100                                  105                                  110  
 Ile Gln Ile Lys Val Ser Thr Pro Pro Pro Gly Thr Ala Ile Arg  
                                   115                                  120  
 Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr Asp Val Val Lys  
                                   130                                  135                                  140  
 Arg Cys Pro Asn His Glu Leu Gly Arg Asp Phe Asn Glu Gly Gln Ser  
   145                                  150                                  155                                  160  
 Ala Pro Ala Ser His Leu Ile Arg Val Glu Gly Asn Asn Leu Ser Gln  
                                   165                                  170                                  175  
 Tyr Val Asp Asp Pro Val Thr Gly Arg Gln Ser Val Val Val Pro Tyr

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180	185	190
Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Ile Leu Tyr Asn Phe 195	200	205
Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu 210	215	220
Ile Ile Ile Thr Leu Glu Met Arg Asp Gly Gln Val Leu Gly Arg Arg 225	230	235
Ser Phe Glu Gly Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala 245	250	255
Asp Glu Asp His Tyr Arg Glu Gln Gln Ala Leu Asn Glu Ser Ser Ala 260	265	270
Lys Asn Gly Ala Ala Ser Lys Arg Ala Phe Lys Gln Ser Pro Pro Ala 275	280	285
Val Pro Ala Leu Gly Ala Gly Val Lys Lys Arg Arg His Gly Asp Glu 290	295	300
Asp Thr Tyr Tyr Leu Gln Val Arg Gly Arg Glu Asn Phe Glu Ile Leu 305	310	315
Met Lys Leu Lys Glu Ser Leu Glu Leu Met Glu Leu Val Pro Gln Pro 325	330	335
Leu Val Asp Ser Tyr Arg Gln Gln Gln Gln Leu Leu Gln Arg Pro Ser 340	345	350
His Leu Gln Pro Pro Ser Tyr Gly Pro Val Leu Ser Pro Met Asn Lys 355	360	365
Val His Gly Gly Met Asn Lys Leu Pro Ser Val Asn Gln Leu Val Gly 370	375	380
Gln Pro Pro Pro His Ser Ser Ala Ala Thr Pro Asn Leu Gly Pro Val 385	390	395
Gly Pro Gly Met Leu Asn Asn His Gly His Ala Val Pro Ala Asn Gly 405	410	415
Glu Met Ser Ser Ser His Ser Ala Gln Ser Met Val Ser Gly Ser His 420	425	430
Cys Thr Pro Pro Pro Pro Tyr His Ala Asp Pro Ser Leu Val Ser Phe 435	440	445
Leu Thr Gly Leu Gly Cys Pro Asn Cys Ile Glu Tyr Phe Thr Ser Gln 450	455	460
Gly Leu Gln Ser Ile Tyr His Leu Gln Asn Leu Thr Ile Glu Asp Leu 465	470	475
Gly Ala Leu Lys Ile Pro Glu Gln Tyr Arg Met Thr Ile Trp Arg Gly 485	490	495

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Leu Gln Asp Leu Lys Gln Gly His Asp Tyr Ser Thr Ala Gln Gln Leu  
500 505 510

Leu Arg Ser Ser Asn Ala Ala Thr Ile Ser Ile Gly Gly Ser Gly Glu  
515 520 525

Leu Gln Arg Gln Arg Val Met Glu Ala Val His Phe Arg Val Arg His  
530 535 540

Thr Ile Thr Ile Pro Asn Arg Gly Gly Pro Gly Gly Gly Pro Asp Glu  
545 550 555 560

Trp Ala Asp Phe Gly Phe Asp Leu Pro Asp Cys Lys Ala Arg Lys Gln  
565 570 575

Pro Ile Lys Glu Glu Phe Thr Glu Ala Glu Ile His  
580 585

&lt;210&gt; 317

&lt;211&gt; 2234

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 317

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aggcactca caggccccag gaaaggccca gccaccgaag ccgctgtggg acagcctgag 2220
tcacctgcag aacc                                     2234

```

&lt;210&gt; 318

&lt;211&gt; 732

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 318

```

Met Pro Glu Glu Thr Gln Thr Gln Asp Gln Pro Met Glu Glu Glu Glu
 1             5             10             15

Val Glu Thr Phe Ala Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu
      20             25             30

Ile Ile Asn Thr Phe Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu
      35             40             45

Ile Ser Asn Ser Ser Asp Ala Leu Asp Lys Ile Arg Tyr Glu Thr Leu
      50             55             60

Thr Asp Pro Ser Lys Leu Asp Ser Gly Lys Glu Leu His Ile Asn Leu
      65             70             75             80

Ile Pro Asn Lys Gln Asp Arg Thr Leu Thr Ile Val Asp Thr Gly Ile
      85             90             95

Gly Met Thr Lys Ala Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys
      100            105            110

Ser Gly Thr Lys Ala Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile
      115            120            125

Ser Met Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val
      130            135            140

Ala Glu Lys Val Thr Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr
      145            150            155            160

Ala Trp Glu Ser Ser Ala Gly Gly Ser Phe Thr Val Arg Thr Asp Thr
      165            170            175

Gly Glu Pro Met Gly Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu
      180            185            190

Asp Gln Thr Glu Tyr Leu Glu Glu Arg Arg Ile Lys Glu Ile Val Lys
      195            200            205

Lys His Ser Gln Phe Ile Gly Tyr Pro Ile Thr Leu Phe Val Glu Lys
      210            215            220

Glu Arg Asp Lys Glu Val Ser Asp Asp Glu Ala Glu Glu Lys Glu Asp
      225            230            235            240

```

275/299

Lys Glu Glu Glu Lys Glu Lys Glu Glu Lys Glu Ser Glu Asp Lys Pro  
 245 250 255  
 Glu Ile Glu Asp Val Gly Ser Asp Glu Glu Glu Glu Lys Lys Asp Gly  
 260 265 270  
 Asp Lys Lys Lys Lys Lys Lys Ile Lys Glu Lys Tyr Ile Asp Gln Glu  
 275 280 285  
 Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp Asp Ile  
 290 295 300  
 Thr Asn Glu Glu Tyr Gly Glu Phe Tyr Lys Ser Leu Thr Asn Asp Trp  
 305 310 315 320  
 Glu Asp His Leu Ala Val Lys His Phe Ser Val Glu Gly Gln Leu Glu  
 325 330 335  
 Phe Arg Ala Leu Phe Val Pro Arg Arg Ala Pro Phe Asp Leu Phe  
 340 345 350  
 Glu Asn Arg Lys Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg Val  
 355 360 365  
 Phe Ile Met Asp Asn Cys Glu Glu Ile Pro Glu Tyr Leu Asn Phe  
 370 375 380  
 Ile Arg Gly Val Val Asp Ser Glu Asp Leu Pro Leu Asn Ile Ser Arg  
 385 390 395 400  
 Glu Met Leu Gln Gln Ser Lys Ile Leu Lys Val Ile Arg Lys Asn Leu  
 405 410 415  
 Val Lys Lys Cys Leu Glu Leu Phe Thr Glu Leu Ala Glu Asp Lys Glu  
 420 425 430  
 Asn Tyr Lys Lys Phe Tyr Glu Gln Phe Ser Lys Asn Ile Lys Leu Gly  
 435 440 445  
 Ile His Glu Asp Ser Gln Asn Arg Lys Lys Leu Ser Glu Leu Leu Arg  
 450 455 460  
 Tyr Tyr Thr Ser Ala Ser Gly Asp Glu Met Val Ser Leu Lys Asp Tyr  
 465 470 475 480  
 Cys Thr Arg Met Lys Glu Asn Gln Lys His Ile Tyr Tyr Ile Thr Gly  
 485 490 495  
 Glu Thr Lys Asp Gln Val Ala Asn Ser Ala Phe Val Glu Arg Leu Arg  
 500 505 510  
 Lys His Gly Leu Glu Val Ile Tyr Met Ile Glu Pro Ile Asp Glu Tyr  
 515 520 525  
 Cys Val Gln Gln Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Ser Val  
 530 535 540

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Thr Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu Glu Glu Lys Lys Lys  
 545 550 555 560  
 Gln Glu Glu Lys Lys Thr Lys Phe Glu Asn Leu Cys Lys Ile Met Lys  
 565 570 575  
 Asp Ile Leu Glu Lys Lys Val Glu Lys Val Val Val Ser Asn Arg Leu  
 580 585 590  
 Val Thr Ser Pro Cys Cys Ile Val Thr Ser Thr Tyr Gly Trp Thr Ala  
 595 600 605  
 Asn Met Glu Arg Ile Met Lys Ala Gln Ala Leu Arg Asp Asn Ser Thr  
 610 615 620  
 Met Gly Tyr Met Ala Ala Lys Lys His Leu Glu Ile Asn Pro Asp His  
 625 630 635 640  
 Ser Ile Ile Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn Asp  
 645 650 655  
 Lys Ser Val Lys Asp Leu Val Ile Leu Leu Tyr Glu Thr Ala Leu Leu  
 660 665 670  
 Ser Ser Gly Phe Ser Leu Glu Asp Pro Gln Thr His Ala Asn Arg Ile  
 675 680 685  
 Tyr Arg Met Ile Lys Leu Gly Leu Gly Ile Asp Glu Asp Asp Pro Thr  
 690 695 700  
 Ala Asp Asp Thr Ser Ala Ala Val Thr Glu Glu Met Pro Pro Leu Glu  
 705 710 715 720  
 Gly Asp Asp Asp Thr Ser Arg Met Glu Glu Val Asp  
 725 730

&lt;210&gt; 319

&lt;211&gt; 249

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 319

Met Lys Glu Thr Gln Lys Ser Thr Tyr Tyr Ile Thr Gly Glu Ser Lys  
 1 5 10 15  
 Glu Gln Val Ala Asn Ser Ala Phe Val Glu Arg Val Arg Lys Gln Gly  
 20 25 30  
 Phe Glu Val Val Tyr Met Thr Glu Pro Ile Asp Glu Tyr Cys Val Gln  
 35 40 45  
 Gln Leu Lys Glu Phe Asp Gly Lys Ser Leu Val Ser Val Thr Lys Glu  
 50 55 60  
 Gly Leu Glu Leu Pro Glu Asp Glu Glu Glu Lys Lys Lys Met Glu Glu  
 65 70 75 80

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Ser Lys Glu Lys Phe Glu Asn Leu Cys Lys Leu Met Lys Glu Ile Leu  
85 90 95

Asp Lys Lys Val Glu Lys Val Thr Ile Ser Asn Arg Leu Val Ser Ser  
100 105 110

Pro Cys Cys Ile Val Thr Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu  
115 120 125

Gln Ile Met Lys Ala Gln Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr  
130 135 140

Met Met Ala Lys Lys His Leu Glu Ile Asn Pro Asp His Pro Ile Met  
145 150 155 160

Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn Asp Lys Ala Val  
165 170 175

Lys Asp Leu Val Val Leu Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly  
180 185 190

Phe Ser Leu Glu Asp Pro Gln Thr His Ser Asn His Ile Tyr His Met  
195 200 205

Ile Lys Leu Gly Leu Gly Thr Asp Glu Asp Glu Val Ala Ala Glu Glu  
210 215 220

Pro Ser Asp Ala Val Pro Asp Glu Ile Pro Pro Leu Glu Gly Asp Glu  
225 230 235 240

Asp Ala Ser Arg Met Glu Glu Val Asp  
245

&lt;210&gt; 320

&lt;211&gt; 1313

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 320

tggtgtggtt gactctgagg atctgcccct gaacatctgc cgagagatgc tccagcagag 60  
caaatctctg aaagtcattc gcaaaaacat tgtaagaagc tgccttgagc tcttctctga 120  
gtggcagaga gacaaggaga ttataagaaa ttctatgagg cattttctaa aaatctcaag 180  
cttggaaatcc acgaagactc cactaacccg caccgcctgt ctgagctgct gcgctgtcac 240  
acctccagc ctggagatga gatgacatct ctgtcgtagt atgtttctca catgaaggag 300  
accagaagat cacactatta catcactggt gagagcaaac agcagggtggc caactctgct 360  
tttgtggagc gagtgcggaa acagggcttc gaggtggtat atatgactga gccattgac 420  
gagtactgtg tgcagcagct caaggagttt gatgggaaaa gcctggtctc agttaccaag 480  
gagggtctgg agctacctga ggatgaggag gagaagaaga agatggaaga aagcaaggaa 540  
aagtttgaga acctctgcaa gctcatgaaa gaaatcttag ataaagaagt tgagaaggtg 600  
acaatctcca atagacttgt gtcttcaccc tgctgcattg tgaccagcac ctacgcgtgg 660  
acagccaata tggagcagat catgaaaagcc caggcacttc gggacaactc caccatgggc 720  
tatatgatgg ccaaaaagca cctggagatc aaccccgacc accccatcat ggagagcgtg 780  
cggcagaagg ctgaggccga caagaatgat aaggcagtta aggacctggt ggtgctgctg 840  
tttgaaccgc cctgctcttc ttccggcttt tcccttgagg atccccagac ccaactccaac 900  
cacactcacc acatgatcaa gctaggtcta ggtactgatg aagatgaagt ggcagcagag 960  
gaaccagctg atgcagttcc tgatgatgac cccctctgt agggatgata ggatgcgtct 1020  
cgcatggaag aagtcgatta ggagttcata gttggaanaac ttgtgccctt gatatggtgc 1080

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```

ccccgggtcc ccaactgcagc ctcgagtgccc cctgtcccac ctggctgctg gtgtctagt 1140
tttttttccc tctctgtcc ttgtgttgaa ggcaggaaac caagggtgtc aagcccccatt 1200
ccctctctac tcttgacagc aggattggat gttgtgtatt gtggtttatt ttattttctt 1260
cattttgttc tgaaattaaa gaatgtaaaa taaagaatat gccgttttta tac 1313

```

&lt;210&gt; 321

&lt;211&gt; 724

&lt;212&gt; PRT

&lt;213&gt; Mus musculus

&lt;400&gt; 321

```

Met Pro Glu Glu Val His His Gly Glu Glu Glu Val Glu Thr Phe Ala
  1                      5                      10          15

```

```

Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe
                20                      25          30

```

```

Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser
  35                      40          45

```

```

Asp Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Ser Lys
  50                      55          60

```

```

Leu Asp Ser Gly Lys Glu Leu Lys Ile Asp Ile Leu Pro Asn Pro Gln
  65                      70          75          80

```

```

Glu Arg Thr Leu Thr Leu Val Asp Thr Gly Ile Gly Met Thr Lys Ala
  85                      90          95

```

```

Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala
  100                     105          110

```

```

Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln
  115                     120          125

```

```

Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Lys Val Val
  130                     135          140

```

```

Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr Ala Trp Glu Ser Ser
  145                     150          155          160

```

```

Ala Gly Gly Ser Phe Thr Val Arg Ala Asp His Gly Glu Pro Ile Gly
  165                     170          175

```

```

Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu Asp Gln Thr Glu Tyr
  180                     185          190

```

```

Leu Glu Glu Arg Arg Val Lys Glu Val Val Lys Lys His Ser Gln Phe
  195                     200          205

```

```

Ile Gly Tyr Pro Ile Thr Leu Tyr Leu Glu Lys Glu Arg Glu Lys Glu
  210                     215          220

```

```

Ile Ser Asp Asp Glu Ala Glu Glu Glu Lys Gly Glu Lys Glu Glu Glu
  225                     230          235          240

```

```

Asp Lys Glu Asp Glu Glu Lys Pro Lys Ile Glu Asp Val Gly Ser Asp

```

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										245					250					255					
Glu	Glu	Asp	Asp	Ser	Gly	Lys	Asp	Lys	Lys	Lys	Lys	Thr	Lys	Lys	Ile										
										260					265					270					
Lys	Glu	Lys	Tyr	Ile	Asp	Gln	Glu	Glu	Leu	Asn	Lys	Thr	Lys	Pro	Ile										
										275					280					285					
Trp	Thr	Arg	Asn	Pro	Asp	Asp	Ile	Thr	Gln	Glu	Glu	Tyr	Gly	Glu	Phe										
										290					295					300					
Tyr	Lys	Ser	Leu	Thr	Asn	Asp	Trp	Glu	Asp	His	Leu	Ala	Val	Lys	His										
										305					310					315					
Phe	Ser	Val	Glu	Gly	Gln	Leu	Glu	Phe	Arg	Ala	Phe	Leu	Phe	Ile	Pro										
										325					330					335					
Arg	Arg	Ala	Pro	Phe	Asp	Leu	Phe	Glu	Asn	Lys	Lys	Lys	Lys	Asn	Asn										
										340					345					350					
Ile	Lys	Leu	Tyr	Val	Arg	Arg	Val	Phe	Ile	Met	Asp	Ser	Cys	Asp	Glu										
										355					360					365					
Leu	Ile	Pro	Glu	Tyr	Leu	Asn	Phe	Ile	Arg	Gly	Val	Val	Asp	Ser	Glu										
										370					375					380					
Asp	Leu	Pro	Leu	Asn	Ile	Ser	Arg	Glu	Met	Leu	Gln	Gln	Ser	Lys	Ile										
										385					390					395					
Leu	Lys	Val	Ile	Arg	Lys	Asn	Ile	Val	Lys	Lys	Cys	Leu	Glu	Leu	Phe										
										405					410					415					
Ser	Glu	Leu	Ala	Glu	Asp	Lys	Glu	Asn	Tyr	Lys	Lys	Phe	Tyr	Glu	Ala										
										420					425					430					
Phe	Ser	Lys	Asn	Leu	Lys	Leu	Gly	Ile	His	Glu	Asp	Ser	Thr	Asn	Arg										
										435					440					445					
Arg	Arg	Leu	Ser	Glu	Leu	Leu	Arg	Tyr	His	Thr	Ser	Gln	Ser	Gly	Asp										
										450					455					460					
Glu	Met	Thr	Ser	Leu	Ser	Glu	Tyr	Val	Ser	Arg	Met	Lys	Glu	Thr	Gln										
										465					470					475					
Lys	Ser	Ile	Tyr	Tyr	Ile	Thr	Gly	Glu	Ser	Lys	Glu	Gln	Val	Ala	Asn										
										485					490					495					
Pro	Ala	Phe	Val	Glu	Arg	Val	Arg	Lys	Arg	Gly	Phe	Glu	Val	Val	Tyr										
										500					505					510					
Met	Thr	Glu	Pro	Ile	Asp	Glu	Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu	Phe										
										515					520					525					
Asp	Gly	Lys	Ser	Leu	Val	Ser	Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu	Pro										
										530					535					540					
Glu	Asp	Glu	Glu	Glu	Lys	Lys	Lys	Met	Glu	Glu	Ser	Lys	Ala	Lys	Phe										
										545					550					555					
										560					565					570					

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Glu Asn Leu Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu  
 565 570 575  
 Lys Val Thr Ile Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val  
 580 585 590  
 Thr Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala  
 595 600 605  
 Gln Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys  
 610 615 620  
 His Leu Glu Ile Asn Pro Asp His Pro Ile Val Glu Thr Leu Arg Gln  
 625 630 635 640  
 Lys Ala Glu Ala Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Val  
 645 650 655  
 Leu Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Glu Asp  
 660 665 670  
 Pro Gln Thr His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu  
 675 680 685  
 Gly Ile Asp Glu Asp Glu Val Thr Ala Glu Glu Pro Ser Ala Ala Val  
 690 695 700  
 Pro Asp Glu Ile Pro Pro Leu Glu Gly Asp Glu Asp Ala Ser Arg Met  
 705 710 715 720  
 Glu Glu Val Asp

&lt;210&gt; 322

&lt;211&gt; 724

&lt;212&gt; PRT

&lt;213&gt; Rattus sp.

&lt;400&gt; 322

Met Pro Glu Glu Val His His Gly Glu Glu Glu Val Glu Thr Phe Ala  
 1 5 10 15  
 Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe  
 20 25 30  
 Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser  
 35 40 45  
 Asp Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Ser Lys  
 50 55 60  
 Leu Asp Ser Gly Lys Glu Leu Lys Ile Asp Ile Ile Pro Asn Pro Gln  
 65 70 75 80  
 Glu Ala Thr Leu Thr Leu Val Asp Thr Gly Ile Gly Met Thr Lys Ala  
 85 90 95

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Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala  
 100 105 110  
 Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln  
 115 120 125  
 Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Lys Val Val  
 130 135 140  
 Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr Ala Trp Glu Ser Ser  
 145 150 155 160  
 Ala Gly Gly Ser Phe Thr Val Arg Ala Asp His Gly Glu Pro Ile Gly  
 165 170 175  
 Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu Asp Gln Thr Glu Tyr  
 180 185 190  
 Leu Glu Glu Arg Arg Val Lys Glu Val Val Lys Lys His Ser Gln Phe  
 195 200 205  
 Ile Gly Tyr Pro Ile Thr Leu Tyr Leu Glu Lys Glu Arg Glu Lys Glu  
 210 215 220  
 Ile Ser Asp Asp Glu Ala Glu Glu Glu Lys Gly Glu Lys Glu Glu Glu  
 225 230 235 240  
 Asp Lys Glu Asp Glu Glu Lys Pro Lys Ile Glu Asp Val Gly Ser Asp  
 245 250 255  
 Glu Glu Asp Asp Ser Gly Lys Asp Lys Lys Lys Thr Lys Lys Ile  
 260 265 270  
 Lys Glu Lys Tyr Ile Asp Gln Glu Glu Leu Asn Lys Thr Lys Pro Ile  
 275 280 285  
 Trp Thr Arg Asn Pro Asp Asp Ile Thr Gln Glu Glu Tyr Gly Glu Phe  
 290 295 300  
 Tyr Lys Ser Leu Thr Asn Asp Trp Glu Asp His Leu Ala Val Lys His  
 305 310 315 320  
 Phe Ser Val Glu Gly Gln Leu Glu Phe Arg Ala Leu Leu Phe Ile Pro  
 325 330 335  
 Arg Arg Ala Pro Phe Asp Leu Phe Glu Asn Lys Lys Lys Asn Asn  
 340 345 350  
 Ile Lys Leu Tyr Val Arg Arg Val Phe Ile Met Asp Ser Cys Asp Asp  
 355 360 365  
 Leu Ile Pro Glu Tyr Leu Asn Phe Ile Arg Gly Val Val Asp Ser Glu  
 370 375 380  
 Asp Leu Pro Leu Asn Ile Ser Arg Glu Met Leu Gln Gln Ser Lys Ile  
 385 390 395 400  
 Leu Lys Val Ile Arg Lys Asn Ile Val Lys Lys Cys Leu Glu Leu Phe



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405										410					415				
Ser	Glu	Leu	Ala	Glu	Asp	Lys	Glu	Asn	Tyr	Lys	Lys	Phe	Tyr	Glu	Ala				
420								425				430							
Phe	Ser	Lys	Asn	Leu	Lys	Leu	Gly	Ile	His	Glu	Asp	Ser	Thr	Asn	Arg				
435				440				445											
Arg	Arg	Leu	Ser	Glu	Leu	Leu	Arg	Tyr	His	Thr	Ser	Gln	Ser	Gly	Asp				
450				455				460											
Glu	Met	Thr	Ser	Leu	Ser	Glu	Tyr	Val	Ser	Arg	Met	Lys	Glu	Thr	Gln				
465				470				475				480							
Lys	Ser	Ile	Tyr	Tyr	Ile	Thr	Gly	Glu	Ser	Lys	Glu	Gln	Val	Ala	Asn				
485				490				495											
Ser	Ala	Phe	Val	Glu	Arg	Val	Arg	Lys	Arg	Gly	Phe	Glu	Val	Val	Tyr				
500				505				510											
Met	Thr	Glu	Pro	Ile	Asp	Glu	Tyr	Cys	Val	Gln	Gln	Leu	Lys	Glu	Phe				
515				520				525											
Asp	Gly	Lys	Ser	Leu	Val	Ser	Val	Thr	Lys	Glu	Gly	Leu	Glu	Leu	Pro				
530				535				540											
Glu	Asp	Glu	Glu	Glu	Lys	Lys	Lys	Met	Glu	Glu	Ser	Lys	Ala	Arg	Phe				
545				550				555				560							
Glu	Asn	Leu	Cys	Lys	Leu	Met	Lys	Glu	Ile	Leu	Asp	Lys	Lys	Val	Glu				
565				570				575											
Lys	Val	Thr	Ile	Ser	Asn	Arg	Leu	Val	Ser	Ser	Pro	Cys	Cys	Ile	Val				
580				585				590											
Thr	Ser	Thr	Tyr	Gly	Trp	Thr	Ala	Asn	Met	Glu	Arg	Ile	Met	Lys	Ala				
595				600				605											
Gln	Ala	Leu	Arg	Asp	Asn	Ser	Thr	Met	Gly	Tyr	Met	Met	Ala	Lys	Lys				
610				615				620											
His	Leu	Glu	Ile	Asn	Pro	Asp	His	Pro	Ile	Val	Glu	Thr	Leu	Arg	Gln				
625				630				635				640							
Lys	Ala	Glu	Ala	Asp	Lys	Asn	Asp	Lys	Ala	Val	Lys	Asp	Leu	Val	Val				
645				650				655											
Leu	Leu	Phe	Glu	Thr	Ala	Leu	Ser	Ser	Leu	Ala	Ser	His	Phe	Arg	Arg				
660				665				670											
Pro	Lys	Thr	His	Ser	Asn	Arg	Ile	Tyr	Arg	Met	Ile	Lys	Leu	Gly	Leu				
675				680				685											
Gly	Ile	Asp	Glu	Asp	Glu	Val	Thr	Ala	Glu	Glu	Pro	Ser	Ala	Ala	Val				
690				695				700											
Pro	Asp	Glu	Ile	Pro	Pro	Leu	Glu	Gly	Asp	Glu	Asp	Ala	Ser	Arg	Met				
705				710				715				720							

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Glu Glu Val Asp

&lt;210&gt; 323

&lt;211&gt; 733

&lt;212&gt; PRT

<213> *Cricetulus griseus*

&lt;400&gt; 323

Met Pro Glu Glu Thr Gln Thr Gln Asp Gln Pro Met Glu Glu Glu Glu  
 1 5 10 15

Val Glu Thr Phe Ala Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu  
 20 25 30

Ile Ile Asn Thr Phe Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu  
 35 40 45

Ile Ser Asn Ser Ser Asp Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu  
 50 55 60

Thr Asp Pro Ser Lys Leu Asp Ser Gly Lys Glu Leu His Ile Asn Ile  
 65 70 75 80

Ile Pro Asn Lys Gln Asp Arg Thr Leu Thr Ile Val Asp Thr Gly Ile  
 85 90 95

Gly Met Thr Lys Ala Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys  
 100 105 110

Ser Gly Thr Lys Ala Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile  
 115 120 125

Ser Met Ile Gly Gln Phe Gly Val Gly Phe Tyr Thr Ala Tyr Leu Val  
 130 135 140

Ala Glu Lys Val Thr Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr  
 145 150 155 160

Ala Trp Glu Ser Ser Ala Gly Gly Ser Phe Thr Val Arg Thr Asp Thr  
 165 170 175

Gly Glu Pro Met Gly Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu  
 180 185 190

Asp Gln Thr Glu Tyr Met Glu Glu Arg Arg Ile Lys Glu Ile Val Lys  
 195 200 205

Lys His Ser Gln Phe Ile Gly Tyr Pro Ile Thr Leu Phe Val Glu Lys  
 210 215 220

Glu Arg Asp Lys Glu Val Ser Asp Asp Glu Ala Glu Glu Lys Glu Asp  
 225 230 235 240

Lys Glu Glu Glu Lys Glu Lys Glu Glu Lys Gly Ile Asp Asp Lys Pro  
 245 250 255

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Glu Ile Glu Asp Val Gly Ser Asp Glu Glu Glu Glu Glu Lys Lys Asp  
 260 265 270  
 Gly Asp Lys Lys Lys Lys Lys Ile Lys Glu Lys Tyr Ile Asp Gln  
 275 280 285  
 Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp Asp  
 290 295 300  
 Ile Thr Asn Glu Glu Tyr Gly Glu Phe Tyr Lys Ser Leu Thr Asn Asp  
 305 310 315 320  
 Trp Glu Glu His Leu Ala Val Lys His Phe Ser Val Glu Gly Gln Leu  
 325 330 335  
 Glu Phe Arg Ala Leu Leu Phe Val Pro Arg Arg Ala Pro Phe Asp Leu  
 340 345 350  
 Phe Glu Asn Arg Lys Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg  
 355 360 365  
 Val Phe Ile Met Asp Asn Cys Glu Glu Leu Phe Pro Glu Tyr Leu Asn  
 370 375 380  
 Phe Ile Arg Gly Val Val Asp Ser Glu Asp Leu Pro Leu Asn Ile Ser  
 385 390 395 400  
 Arg Glu Ile Leu Gln Gln Ser Lys Ile Leu Lys Val Ile Arg Lys Asn  
 405 410 415  
 Leu Val Arg Lys Cys Leu Glu Leu Phe His Glu Leu Ala Glu Asp Lys  
 420 425 430  
 Glu Asn Tyr Lys Lys Phe Tyr Glu Gln Phe Ser Lys Asn Ile Lys Leu  
 435 440 445  
 Gly Ile His Glu Asp Ser Gln Asn Arg Lys Lys Leu Ser Glu Leu Leu  
 450 455 460  
 Arg Tyr Tyr Thr Ser Ala Ser Gly Asp Glu Met Val Ser Leu Lys Asp  
 465 470 475 480  
 Tyr Cys Thr Arg Met Lys Glu Asn Gln Lys His Ile Tyr Phe Ile Thr  
 485 490 495  
 Gly Glu Thr Lys Asp Gln Val Ala Asn Ser Ala Phe Val Glu Arg Leu  
 500 505 510  
 Arg Lys His Gly Leu Glu Val Ile Tyr Met Ile Glu Pro Ile Asp Glu  
 515 520 525  
 Tyr Cys Val Gln Gln Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Ser  
 530 535 540  
 Val Thr Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu Glu Glu Lys Lys  
 545 550 555 560  
 Lys Gln Glu Glu Lys Lys Thr Lys Phe Glu Asn Leu Cys Lys Ile Met

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565                      570                      575  
 Lys Asp Ile Leu Glu Lys Lys Val Glu Lys Val Val Val Ser Asn Arg  
                          580                      585                      590  
 Leu Val Thr Ser Pro Cys Cys Ile Val Thr Ser Thr Tyr Gly Trp Thr  
                          595                      600                      605  
 Ala Asn Met Glu Arg Ile Ile Lys Ala Gln Ala Leu Arg Asp Asn Ser  
                          610                      615                      620  
 Thr Met Gly Tyr Met Ala Ala Lys Lys His Leu Glu Ile Asn Pro Asp  
                          625                      630                      635                      640  
 His Ser Ile Ile Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn  
                          645                      650                      655  
 Asp Lys Ser Val Lys Asp Leu Val Ile Leu Leu Tyr Glu Thr Ala Leu  
                          660                      665                      670  
 Leu Ser Ser Gly Phe Ser Leu Glu Asp Pro Gln Thr His Ala Asn Arg  
                          675                      680                      685  
 Ile Tyr Arg Met Ile Lys Leu Gly Leu Gly Ile Asp Glu Asp Asp Pro  
                          690                      695                      700  
 Thr Val Asp Asp Thr Ser Ala Ala Val Thr Glu Glu Met Pro Pro Leu  
                          705                      710                      715                      720  
 Glu Gly Asp Asp Asp Thr Ser Arg Met Glu Glu Val Asp  
                          725                      730

&lt;210&gt; 324

&lt;211&gt; 725

&lt;212&gt; PRT

&lt;213&gt; Gallus gallus

&lt;400&gt; 324

Met Pro Glu Gln Val Gln His Gly Glu Asp Glu Val Glu Thr Phe Ala  
                          1                      5                      10                      15  
 Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe  
                          20                      25                      30  
 Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser  
                          35                      40                      45  
 Asp Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Ser Lys  
                          50                      55                      60  
 Leu Asp Thr Gly Lys Asp Leu Lys Ile Asp Ile Val Pro Asn Pro Arg  
                          65                      70                      75                      80  
 Asp Pro Thr Leu Thr Leu Leu Asp Thr Gly Ile Gly Met Thr Lys Ala  
                          85                      90                      95  
 Asp Leu Val Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala

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100	105	110
Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln 115 120 125		
Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Lys Val Val 130 135 140		
Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr Ala Trp Glu Ser Ser 145 150 155 160		
Ala Gly Gly Ser Phe Thr Val Arg Thr Asp His Gly Glu Pro Ile Gly 165 170 175		
Arg Gly Thr Lys Val Ile Leu Tyr Leu Lys Glu Asp Gln Thr Glu Tyr 180 185 190		
Leu Glu Glu Arg Arg Val Lys Glu Val Val Lys Lys His Ser Gln Phe 195 200 205		
Ile Gly Tyr Pro Ile Thr Leu Tyr Val Glu Lys Glu Arg Glu Lys Glu 210 215 220		
Val Ser Asp Asp Glu Ala Glu Glu Glu Lys Val Glu Lys Glu Glu Glu 225 230 235 240		
Glu Ser Lys Asp Glu Glu Lys Pro Lys Ile Glu Asp Val Gly Ser Asp 245 250 255		
Glu Glu Glu Glu Glu Gly Glu Lys Ser Lys Lys Lys Lys Thr Lys Lys 260 265 270		
Ile Lys Glu Lys Tyr Ile Asp Gln Glu Glu Leu Asn Lys Thr Lys Pro 275 280 285		
Ile Trp Thr Arg Asn Pro Asp Asp Ile Thr Gln Glu Glu Tyr Gly Glu 290 295 300		
Phe Tyr Lys Ser Leu Thr Asn Asp Trp Glu Asp His Leu Ala Val Lys 305 310 315 320		
His Phe Ser Val Glu Gly Gln Leu Glu Phe Arg Ala Leu Leu Phe Ile 325 330 335		
Pro Arg Arg Ala Pro Phe Asp Leu Phe Glu Asn Lys Lys Lys Lys Asn 340 345 350		
Asn Ile Lys Leu Tyr Val Arg Arg Val Phe Ile Met Asp Ser Cys Asp 355 360 365		
Glu Leu Ile Pro Glu Tyr Leu Asn Phe Ile Arg Gly Val Val Asp Ser 370 375 380		
Glu Asp Leu Pro Leu Asn Ile Ser Arg Glu Met Leu Gln Gln Ser Lys 385 390 395 400		
Ile Leu Lys Val Ile Arg Lys Asn Ile Val Lys Lys Cys Leu Glu Leu 405 410 415		

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Phe Thr Glu Leu Ala Glu Asp Lys Glu Asn Tyr Lys Lys Phe Tyr Glu  
 420 425 430  
 Ala Phe Ser Lys Asn Leu Lys Leu Gly Ile His Glu Asp Ser Thr Asn  
 435 440 445  
 Arg Lys Arg Leu Ser Glu Leu Leu Arg Tyr His Thr Ser Gln Ser Gly  
 450 455 460  
 Asp Glu Met Thr Ser Leu Ser Glu Tyr Val Ser Arg Met Lys Glu Ser  
 465 470 475 480  
 Gln Lys Ser Ile Tyr Tyr Ile Thr Gly Glu Ser Lys Glu Gln Val Ala  
 485 490 495  
 Asn Ser Ala Phe Val Glu Arg Val Arg Lys Arg Gly Phe Glu Val Val  
 500 505 510  
 Tyr Met Thr Glu Pro Ile Asp Glu Tyr Cys Val Gln Gln Leu Lys Glu  
 515 520 525  
 Phe Asp Gly Lys Thr Leu Val Ser Val Thr Lys Glu Gly Leu Glu Leu  
 530 535 540  
 Pro Glu Asp Glu Glu Lys Lys Asn Met Glu Glu Ser Lys Ala Lys  
 545 550 555 560  
 Phe Glu Thr Leu Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val  
 565 570 575  
 Glu Lys Val Thr Ile Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile  
 580 585 590  
 Val Thr Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys  
 595 600 605  
 Ala Gln Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys  
 610 615 620  
 Lys His Leu Glu Ile Asn Pro Asp His Pro Ile Val Glu Thr Leu Arg  
 625 630 635 640  
 Gln Lys Ala Asp Ala Asn Lys Asn Asp Lys Ala Val Lys Asp Leu Val  
 645 650 655  
 Val Leu Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Glu  
 660 665 670  
 Asp Pro Gln Thr His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly  
 675 680 685  
 Leu Gly Ile Asp Glu Asp Glu Val Ile Ala Glu Glu Ser Ser Ile Ala  
 690 695 700  
 Pro Pro Asp Glu Ile Pro Pro Leu Glu Gly Asp Glu Asp Thr Ser Arg  
 705 710 715 720

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Met Glu Glu Val Asp  
725

<210> 325  
<211> 233  
<212> PRT  
<213> *Sarcophaga crassipalpis*

<400> 325

Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Asp Lys Val Thr  
1 5 10 15

Val Thr Ser Lys His Asn Asp Asp Glu Gln Tyr Ile Trp Glu Ser Ser  
20 25 30

Ala Gly Gly Ser Phe Thr Val Lys Pro Asp Ser Ser Glu Pro Leu Gly  
35 40 45

Arg Gly Thr Lys Ile Val Leu Tyr Ile Lys Glu Asp Gln Thr Glu Tyr  
50 55 60

Leu Glu Glu Ser Lys Ile Lys Glu Ile Val Asn Lys His Ser Gln Phe  
65 70 75 80

Ile Gly Tyr Pro Ile Lys Leu Leu Val Gln Lys Glu Arg Asp Gln Glu  
85 90 95

Val Ser Asp Asp Glu Ala Glu Glu Glu Lys Lys Glu Met Asp Thr Asp  
100 105 110

Glu Pro Lys Ile Glu Asp Val Gly Glu Asp Glu Asp Ala Asp Lys Lys  
115 120 125

Asp Lys Asp Gly Lys Lys Lys Lys Thr Ile Lys Val Ala Tyr Thr Glu  
130 135 140

Asp Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp  
145 150 155 160

Asp Ile Thr Gln Ala Glu Tyr Gly Asp Phe Tyr Lys Ser Leu Thr Asn  
165 170 175

Asp Trp Glu Asp His Leu Ala Val Lys His Phe Pro Leu Lys Gly Gln  
180 185 190

Leu Glu Phe Arg Ala Leu Leu Phe Ile Pro Arg Arg Thr Pro Phe Asp  
195 200 205

Leu Phe Glu Asn Gln Lys Lys Arg Asn Asn Ile Lys Leu Tyr Val Pro  
210 215 220

Arg Val Phe Ile Met Asp Asn Cys Glu  
225 230

<210> 326  
<211> 724

289/299

&lt;212&gt; PRT

&lt;213&gt; Danio rerio

&lt;400&gt; 326

Met Pro Glu Glu Met Arg Gln Glu Glu Glu Ala Glu Thr Phe Ala Phe  
 1 5 10 15

Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe Tyr  
 20 25 30

Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Val Ser Asn Ala Ser Asp  
 35 40 45

Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Thr Lys Leu  
 50 55 60

Asp Ser Gly Lys Asp Leu Lys Ile Asp Ile Ile Pro Asn Val Gln Glu  
 65 70 75 80

Arg Thr Leu Thr Leu Ile Asp Thr Gly Ile Gly Met Thr Lys Ala Asp  
 85 90 95

Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala Phe  
 100 105 110

Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln Phe  
 115 120 125

Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Lys Val Thr Val  
 130 135 140

Ile Thr Lys His Asn Asp Asp Glu Gln Tyr Ala Trp Glu Ser Ser Ala  
 145 150 155 160

Gly Gly Ser Phe Thr Val Lys Val Asp His Gly Glu Pro Ile Gly Arg  
 165 170 175

Gly Thr Lys Val Ile Leu His Leu Lys Glu Asp Gln Thr Glu Tyr Ile  
 180 185 190

Glu Glu Lys Arg Val Lys Glu Val Val Lys Lys His Ser Gln Phe Ile  
 195 200 205

Gly Tyr Pro Ile Thr Leu Tyr Val Glu Lys Glu Arg Asp Lys Glu Ile  
 210 215 220

Ser Asp Asp Glu Ala Glu Glu Glu Lys Ala Glu Lys Glu Glu Lys Glu  
 225 230 235 240

Glu Glu Gly Glu Asp Lys Pro Lys Ile Glu Asp Val Gly Ser Asp Asp  
 245 250 255

Glu Glu Asp Thr Lys Asp Lys Asp Lys Lys Lys Lys Lys Ile Lys  
 260 265 270

Glu Lys Tyr Ile Asp Gln Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp  
 275 280 285



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Thr Arg Asn Pro Asp Asp Ile Ser Asn Glu Glu Tyr Gly Glu Phe Tyr  
 290 295 300  
 Lys Ser Leu Thr Asn Asp Trp Glu Asp His Leu Ala Val Lys His Phe  
 305 310 315 320  
 Ser Val Glu Gly Gln Leu Glu Phe Arg Ala Leu Leu Phe Ile Pro Arg  
 325 330 335  
 Arg Ala Pro Phe Asp Leu Phe Glu Asn Lys Lys Lys Lys Asn Asn Ile  
 340 345 350  
 Lys Leu Tyr Val Arg Arg Val Phe Ile Met Asp Asn Cys Glu Glu Leu  
 355 360 365  
 Ile Pro Glu Tyr Leu Asn Phe Ile Arg Gly Val Val Asp Ser Glu Asp  
 370 375 380  
 Leu Pro Leu Asn Ile Ser Arg Glu Met Leu Gln Gln Ser Lys Ile Leu  
 385 390 395 400  
 Lys Val Ile Arg Lys Asn Ile Val Lys Lys Cys Leu Glu Leu Phe Ala  
 405 410 415  
 Asp Val Ala Glu Asp Lys Asp Asn Tyr Lys Lys Phe Tyr Asp Ala Phe  
 420 425 430  
 Ser Lys Asn Leu Lys Leu Gly Ile His Glu Asp Ser Gln Asn Arg Arg  
 435 440 445  
 Lys Leu Ser Glu Leu Leu Arg Tyr Gln Ser Ser Gln Ser Gly Tyr Glu  
 450 455 460  
 Met Thr Ser Leu Thr Glu Tyr Val Ser Arg Met Lys Glu Asn Gln Lys  
 465 470 475 480  
 Ser Ile Tyr Tyr Ile Thr Gly Glu Ser Lys Asp Gln Val Ala His Ser  
 485 490 495  
 Ala Phe Val Glu Arg Val Cys Lys Arg Gly Phe Glu Val Leu Tyr Met  
 500 505 510  
 Thr Glu Pro Ile Asp Glu Tyr Cys Val Gln Gln Leu Lys Asp Phe Asp  
 515 520 525  
 Gly Lys Ser Leu Val Ser Val Thr Lys Glu Gly Leu Glu Leu Pro Glu  
 530 535 540  
 Asp Glu Asp Glu Lys Lys Lys Met Glu Glu Asp Lys Ala Lys Phe Glu  
 545 550 555 560  
 Asn Leu Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu Lys  
 565 570 575  
 Val Thr Val Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val Thr  
 580 585 590  
 Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala Gln

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595                      600                      605  
 Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys His  
 610                      615                      620  
 Leu Glu Ile Asn Pro Asp His Pro Ile Met Glu Thr Leu Arg Gln Lys  
 625                      630                      635                      640  
 Ala Glu Ala Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Ile Leu  
 645                      650                      655  
 Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Asp Asp Pro  
 660                      665                      670  
 Gln Thr His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu Gly  
 675                      680                      685  
 Ile Asp Glu Asp Glu Asp Val Pro Val Glu Glu Pro Ser Ser Ala Ala  
 690                      695                      700  
 Pro Glu Asp Ile Pro Pro Leu Glu Gly Asp Asp Asp Ala Ser Arg Met  
 705                      710                      715                      720  
 Glu Glu Val Asp  
  
 <210> 327  
 <211> 722  
 <212> PRT  
 <213> Salmo salar  
  
 <400> 327  
 Met Pro Glu Glu Met Arg Gln Glu Glu Glu Ala Glu Thr Phe Ala Phe  
 1                      5                      10                      15  
 Gln Ala Glu Ile Ala Gln Leu Met Ser Leu Ile Ile Asn Thr Phe Tyr  
 20                      25                      30  
 Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu Ile Ser Asn Ala Ser Asp  
 35                      40                      45  
 Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu Thr Asp Pro Thr Lys Leu  
 50                      55                      60  
 Asp Asn Gly Lys Glu Leu Lys Ile Asp Val Ile Pro Asn Val Glu Glu  
 65                      70                      75                      80  
 Arg Thr Leu Thr Leu Ile Asp Thr Gly Ile Gly Met Thr Lys Ala Asp  
 85                      90                      95  
 Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys Ser Gly Thr Lys Ala Phe  
 100                      105                      110  
 Met Glu Ala Leu Gln Ala Gly Ala Asp Ile Ser Met Ile Gly Gln Phe  
 115                      120                      125  
 Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val Ala Glu Arg Val Thr Val  
 130                      135                      140

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Ile Thr Lys His Asn Asp Asp Glu Gln Tyr Ile Trp Glu Ser Ser Ala  
 145 150 155 160  
 Gly Gly Ser Phe Thr Val Lys Val Asp Thr Gly Glu Pro Met Leu Arg  
 165 170 175  
 Gly Thr Lys Val Ile Leu His Met Lys Glu Asp Gln Thr Glu Tyr Val  
 180 185 190  
 Glu Glu Lys Arg Val Lys Glu Val Val Lys Lys His Ser Gln Phe Ile  
 195 200 205  
 Gly Tyr Pro Ile Thr Leu Phe Val Glu Lys Glu Arg Glu Lys Glu Ile  
 210 215 220  
 Ser Asp Asp Glu Glu Glu Lys Ala Glu Glu Glu Lys Glu Glu Lys Glu  
 225 230 235 240  
 Ala Glu Asp Lys Pro Lys Ile Glu Asp Val Gly Ser Asp Asp Glu Glu  
 245 250 255  
 Asp Ser Lys Asp Lys Asp Lys Lys Lys Thr Lys Lys Ile Lys Glu Lys  
 260 265 270  
 Tyr Ile Asp Gln Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg  
 275 280 285  
 Asn Pro Asp Asp Ile Thr Met Glu Glu Tyr Gly Glu Phe Tyr Lys Ser  
 290 295 300  
 Leu Thr Asn Asp Trp Glu Glu His Leu Ala Val Lys His Phe Ser Val  
 305 310 315 320  
 Glu Gly Gln Leu Glu Phe Arg Ala Leu Leu Phe Ile Pro Arg Arg Ala  
 325 330 335  
 Pro Phe Asp Leu Phe Glu Asn Lys Lys Lys Lys Asn Asn Ile Lys Leu  
 340 345 350  
 Tyr Val Arg Arg Val Phe Ile Met Asp Ser Cys Glu Glu Leu Ile Pro  
 355 360 365  
 Glu Tyr Leu Asn Phe Val Arg Gly Val Val Asp Ser Glu Asp Leu Pro  
 370 375 380  
 Leu Asn Ile Ser Arg Glu Met Leu Gln Gln Ser Lys Ile Leu Lys Val  
 385 390 395 400  
 Ile Arg Lys Asn Ile Val Lys Lys Cys Met Glu Leu Phe Gly Glu Leu  
 405 410 415  
 Ala Glu Asp Arg Glu Asn Tyr Asn Lys Phe Tyr Asp Gly Phe Ser Lys  
 420 425 430  
 Asn Leu Lys Leu Gly Ile His Glu Asp Ser Gln Asn Arg Lys Lys Leu  
 435 440 445

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Ser Glu Leu Leu Arg Tyr His Ser Ser Gln Ser Gly Asp Glu Leu Thr  
 450 455 460  
 Ser Leu Thr Glu Tyr Leu Thr Arg Met Lys Asp Asn Gln Lys Ser Ile  
 465 470 475 480  
 Tyr Tyr Ile Thr Gly Glu Ser Lys Asp Gln Val Ala Asn Ser Ala Phe  
 485 490 495  
 Val Glu Arg Val Arg Lys Arg Gly Phe Glu Val Leu Tyr Met Thr Glu  
 500 505 510  
 Pro Ile Asp Glu Tyr Cys Val Gln Gln Leu Lys Glu Phe Asp Gly Lys  
 515 520 525  
 Thr Leu Val Ser Val Thr Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu  
 530 535 540  
 Glu Glu Lys Lys Lys Met Asp Glu Asp Lys Thr Lys Phe Glu Asn Leu  
 545 550 555 560  
 Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu Lys Val Thr  
 565 570 575  
 Val Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val Thr Ser Thr  
 580 585 590  
 Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala Gln Ala Leu  
 595 600 605  
 Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys His Leu Glu  
 610 615 620  
 Ile Asn Pro Asp His Pro Ile Val Glu Thr Leu Arg Gln Lys Ala Asp  
 625 630 635 640  
 Leu Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Ile Leu Leu Phe  
 645 650 655  
 Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Asp Asp Pro Gln Thr  
 660 665 670  
 His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu Gly Ile Asp  
 675 680 685  
 Asp Asp Glu Val Ile Pro Glu Glu Pro Thr Ser Ala Pro Ala Pro Asp  
 690 695 700  
 Glu Ile Pro Pro Leu Glu Gly Asp Asp Asp Ala Ser Arg Met Glu Glu  
 705 710 715 720  
 Val Asp

&lt;210&gt; 328

&lt;211&gt; 733

&lt;212&gt; PRT

&lt;213&gt; Sus scrofa

294/299

&lt;400&gt; 328

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Met Pro Glu Glu Thr Gln Thr Gln Asp Gln Pro Met Glu Glu Glu Glu
  1              5              10              15

Val Glu Thr Phe Ala Phe Gln Ala Glu Ile Ala Gln Leu Met Ser Leu
      20              25              30

Ile Ile Asn Thr Phe Tyr Ser Asn Lys Glu Ile Phe Leu Arg Glu Leu
      35              40              45

Ile Ser Asn Ser Ser Asp Ala Leu Asp Lys Ile Arg Tyr Glu Ser Leu
      50              55              60

Thr Asp Pro Ser Lys Leu Asp Ser Gly Lys Glu Leu His Ile Asn Leu
      65              70              75              80

Ile Pro Asn Lys Gln Asp Arg Thr Leu Thr Ile Val Asp Thr Gly Ile
      85              90              95

Gly Met Thr Lys Ala Asp Leu Ile Asn Asn Leu Gly Thr Ile Ala Lys
      100             105             110

Ser Gly Thr Lys Ala Phe Met Glu Ala Leu Gln Ala Gly Ala Asp Ile
      115             120             125

Ser Met Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Ala Tyr Leu Val
      130             135             140

Ala Glu Lys Val Thr Val Ile Thr Lys His Asn Asp Asp Glu Gln Tyr
      145             150             155             160

Ala Trp Glu Ser Ser Ala Gly Gly Ser Phe Thr Val Arg Thr Asp Thr
      165             170             175

Gly Glu Pro Met Gly Arg Gly Thr Lys Val Ile Leu His Leu Lys Glu
      180             185             190

Asp Gln Thr Glu Tyr Leu Glu Glu Arg Arg Ile Lys Glu Ile Val Lys
      195             200             205

Lys His Ser Gln Phe Ile Gly Tyr Pro Ile Thr Leu Phe Val Glu Lys
      210             215             220

Glu Arg Asp Lys Glu Val Ser Asp Asp Glu Ala Glu Glu Lys Glu Asp
      225             230             235             240

Lys Glu Glu Glu Lys Glu Lys Glu Glu Lys Glu Ser Glu Asp Lys Pro
      245             250             255

Glu Ile Glu Asp Val Gly Ser Asp Glu Glu Glu Glu Lys Lys Asp
      260             265             270

Gly Asp Lys Lys Lys Lys Lys Lys Ile Lys Glu Lys Tyr Ile Asp Gln
      275             280             285

Glu Glu Leu Asn Lys Thr Lys Pro Ile Trp Thr Arg Asn Pro Asp Asp
      290             295             300

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Ile Thr Asn Glu Glu Tyr Gly Glu Phe Tyr Lys Ser Leu Thr Asn Asp  
 305 310 315 320  
 Trp Glu Asp His Leu Ala Val Lys His Phe Ser Val Glu Gly Gln Leu  
 325 330 335  
 Glu Phe Arg Ala Leu Leu Phe Val Pro Arg Arg Ala Pro Phe Asp Leu  
 340 345 350  
 Phe Glu Asn Arg Lys Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg  
 355 360 365  
 Val Phe Ile Met Asp Asn Cys Glu Glu Leu Ile Pro Glu Tyr Leu Asn  
 370 375 380  
 Phe Ile Arg Gly Val Val Asp Ser Glu Asp Leu Pro Leu Asn Ile Ser  
 385 390 395 400  
 Arg Glu Met Leu Gln Gln Ser Lys Ile Leu Lys Val Ile Arg Lys Asn  
 405 410 415  
 Leu Val Lys Lys Cys Leu Glu Leu Phe Thr Glu Leu Ala Glu Asp Lys  
 420 425 430  
 Glu Asn Tyr Lys Lys Phe Tyr Glu Gln Phe Ser Lys Asn Ile Lys Leu  
 435 440 445  
 Gly Ile His Glu Asp Ser Gln Asn Arg Lys Lys Leu Ser Glu Leu Leu  
 450 455 460  
 Arg Tyr Tyr Thr Ser Ala Ser Gly Asp Glu Met Val Ser Leu Lys Asp  
 465 470 475 480  
 Tyr Cys Thr Arg Met Lys Glu Asn Gln Lys His Ile Tyr Tyr Ile Thr  
 485 490 495  
 Gly Glu Thr Lys Asp Gln Val Ala Asn Ser Ala Phe Val Glu Arg Leu  
 500 505 510  
 Arg Lys His Gly Leu Glu Val Ile Tyr Met Ile Glu Pro Ile Asp Glu  
 515 520 525  
 Tyr Cys Val Gln Gln Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Ser  
 530 535 540  
 Val Thr Lys Glu Gly Leu Glu Leu Pro Glu Asp Glu Glu Glu Lys Lys  
 545 550 555 560  
 Lys Gln Glu Glu Lys Lys Thr Lys Phe Glu Asn Leu Cys Lys Ile Met  
 565 570 575  
 Lys Asp Ile Leu Glu Lys Lys Val Glu Lys Val Val Ser Asn Arg  
 580 585 590  
 Leu Val Thr Ser Pro Cys Cys Ile Val Thr Ser Thr Tyr Gly Trp Thr  
 595 600 605

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Ala Asn Met Glu Arg Ile Met Lys Ala Gln Ala Leu Arg Asp Asn Ser  
 610 615 620

Thr Met Gly Tyr Met Ala Ala Lys Lys His Leu Glu Ile Asn Pro Asp  
 625 630 635 640

His Ser Ile Ile Glu Thr Leu Arg Gln Lys Ala Glu Ala Asp Lys Asn  
 645 650 655

Asp Lys Ser Val Lys Asp Leu Val Ile Leu Leu Tyr Glu Thr Ala Leu  
 660 665 670

Leu Ser Ser Gly Phe Ser Leu Glu Asp Pro Gln Thr His Ala Asn Arg  
 675 680 685

Ile Tyr Arg Met Ile Lys Leu Gly Leu Gly Ile Asp Glu Asp Asp Pro  
 690 695 700

Thr Ala Asp Asp Ser Ser Ala Ala Val Thr Glu Glu Met Pro Pro Leu  
 705 710 715 720

Glu Gly Asp Asp Asp Thr Ser Arg Met Glu Glu Val Asp  
 725 730

&lt;210&gt; 329

&lt;211&gt; 709

&lt;212&gt; PRT.

<213> *Saccharomyces cerevisiae*

&lt;400&gt; 329

Met Ala Ser Glu Thr Phe Glu Phe Gln Ala Glu Ile Thr Gln Leu Met  
 1 5 10 15

Ser Leu Ile Ile Asn Thr Val Tyr Ser Asn Lys Glu Ile Phe Leu Arg  
 20 25 30

Glu Leu Ile Ser Asn Ala Ser Asp Ala Leu Asp Lys Ile Arg Tyr Lys  
 35 40 45

Ser Leu Ser Asp Pro Lys Gln Leu Glu Thr Glu Pro Asp Leu Phe Ile  
 50 55 60

Arg Ile Thr Pro Lys Pro Glu Gln Lys Val Leu Glu Ile Arg Asp Ser  
 65 70 75 80

Gly Ile Gly Met Thr Lys Ala Glu Leu Ile Asn Asn Leu Gly Thr Ile  
 85 90 95

Ala Lys Ser Gly Thr Lys Ala Phe Met Glu Ala Leu Ser Ala Gly Ala  
 100 105 110

Asp Val Ser Met Ile Gly Gln Phe Gly Val Gly Phe Tyr Ser Leu Phe  
 115 120 125

Leu Val Ala Asp Arg Val Gln Val Ile Ser Lys Ser Asn Asp Asp Glu  
 130 135 140

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Gln Tyr Ile Trp Glu Ser Asn Ala Gly Gly Ser Phe Thr Val Thr Leu  
 145 150 155 160  
 Asp Glu Val Asn Glu Arg Ile Gly Arg Gly Thr Ile Leu Arg Leu Phe  
 165 170 175  
 Leu Lys Asp Asp Gln Leu Glu Tyr Leu Glu Glu Lys Arg Ile Lys Glu  
 180 185 190  
 Val Ile Lys Arg His Ser Glu Phe Val Ala Tyr Pro Ile Gln Leu Val  
 195 200 205  
 Val Thr Lys Glu Val Glu Lys Glu Val Pro Ile Pro Glu Glu Glu Lys  
 210 215 220  
 Lys Asp Glu Glu Lys Lys Asp Glu Glu Lys Lys Asp Glu Asp Asp Lys  
 225 230 235 240  
 Lys Pro Lys Leu Glu Glu Val Asp Glu Glu Glu Lys Lys Pro Lys  
 245 250 255  
 Thr Lys Lys Val Lys Glu Glu Val Gln Glu Ile Glu Glu Leu Asn Lys  
 260 265 270  
 Thr Lys Pro Leu Trp Thr Arg Asn Pro Ser Asp Ile Thr Gln Glu Glu  
 275 280 285  
 Tyr Asn Ala Phe Tyr Lys Ser Ile Ser Asn Asp Trp Glu Asp Pro Leu  
 290 295 300  
 Tyr Val Lys His Phe Ser Val Glu Gly Gln Leu Glu Phe Arg Ala Ile  
 305 310 315 320  
 Leu Phe Ile Pro Lys Arg Ala Pro Phe Asp Leu Phe Glu Ser Lys Lys  
 325 330 335  
 Lys Lys Asn Asn Ile Lys Leu Tyr Val Arg Arg Val Phe Ile Thr Asp  
 340 345 350  
 Glu Ala Glu Asp Leu Ile Pro Glu Trp Leu Ser Phe Val Lys Gly Val  
 355 360 365  
 Val Asp Ser Glu Asp Leu Pro Leu Asn Leu Ser Arg Glu Met Leu Gln  
 370 375 380  
 Gln Asn Lys Ile Met Lys Val Ile Arg Lys Asn Ile Val Lys Lys Leu  
 385 390 395 400  
 Ile Glu Ala Phe Asn Glu Ile Ala Glu Asp Ser Glu Gln Phe Glu Lys  
 405 410 415  
 Phe Tyr Ser Ala Phe Ser Lys Asn Ile Lys Leu Gly Val His Glu Asp  
 420 425 430  
 Thr Gln Asn Arg Ala Ala Leu Ala Lys Leu Leu Arg Tyr Asn Ser Thr  
 435 440 445  
 Lys Ser Val Asp Glu Leu Thr Ser Leu Thr Asp Tyr Val Thr Arg Met



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450                      455                      460  
 Pro Glu His Gln Lys Asn Ile Tyr Tyr Ile Thr Gly Glu Ser Leu Lys  
 465                      470                      475                      480  
 Ala Val Glu Lys Ser Pro Phe Leu Asp Ala Leu Lys Ala Lys Asn Phe  
 485                      490                      495  
 Glu Val Leu Phe Leu Thr Asp Pro Ile Asp Glu Tyr Ala Phe Thr Gln  
 500                      505                      510  
 Leu Lys Glu Phe Glu Gly Lys Thr Leu Val Asp Ile Thr Lys Asp Phe  
 515                      520                      525  
 Glu Leu Glu Glu Thr Asp Glu Glu Lys Ala Glu Arg Glu Lys Glu Ile  
 530                      535                      540  
 Lys Glu Tyr Glu Pro Leu Thr Lys Ala Leu Lys Glu Ile Leu Gly Asp  
 545                      550                      555                      560  
 Gln Val Glu Lys Val Val Val Ser Tyr Lys Leu Leu Asp Ala Pro Ala  
 565                      570                      575  
 Ala Ile Arg Thr Gly Gln Phe Gly Trp Ser Ala Asn Met Glu Arg Ile  
 580                      585                      590  
 Met Lys Ala Gln Ala Leu Arg Asp Ser Ser Met Ser Ser Tyr Met Ser  
 595                      600                      605  
 Ser Lys Lys Thr Phe Glu Ile Ser Pro Lys Ser Pro Ile Ile Lys Glu  
 610                      615                      620  
 Leu Lys Lys Arg Val Asp Glu Gly Gly Ala Gln Asp Lys Thr Val Lys  
 625                      630                      635                      640  
 Asp Leu Thr Lys Leu Leu Tyr Glu Thr Ala Leu Leu Thr Ser Gly Phe  
 645                      650                      655  
 Ser Leu Asp Glu Pro Thr Ser Phe Ala Ser Arg Ile Asn Arg Leu Ile  
 660                      665                      670  
 Ser Leu Gly Leu Asn Ile Asp Glu Asp Glu Thr Glu Thr Ala Pro  
 675                      680                      685  
 Glu Ala Ser Thr Ala Ala Pro Val Glu Glu Val Pro Ala Asp Thr Glu  
 690                      695                      700  
 Met Glu Glu Val Asp  
 705

&lt;210&gt; 330

&lt;211&gt; 260

&lt;212&gt; PRT

&lt;213&gt; Rana esculenta

&lt;400&gt; 330

Glu Met Ala Ser Leu Ser Glu Tyr Val Ser Arg Met Lys Glu Thr Gln

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1	5	10	15
Lys Ser Ile Tyr Tyr Ile Thr Gly Glu Ser Lys Glu Gln Val Ala Asn			
20		25	30
Ser Ala Phe Val Glu Arg Val Arg Lys Arg Gly Phe Glu Val Val Tyr			
35		40	45
Met Thr Glu Pro Ile Asp Glu Tyr Cys Val Gln Gln Leu Lys Glu Phe			
50		55	60
Asp Gly Lys Thr Leu Val Ser Val Thr Lys Glu Gly Leu Glu Leu Pro			
65		70	75
Glu Asp Asp Glu Glu Lys Lys Lys Met Glu Glu Asn Lys Thr Lys Phe			
85		90	95
Glu Gly Leu Cys Lys Leu Met Lys Glu Ile Leu Asp Lys Lys Val Glu			
100		105	110
Lys Val Thr Val Ser Asn Arg Leu Val Ser Ser Pro Cys Cys Ile Val			
115		120	125
Thr Ser Thr Tyr Gly Trp Thr Ala Asn Met Glu Arg Ile Met Lys Ala			
130		135	140
Gln Ala Leu Arg Asp Asn Ser Thr Met Gly Tyr Met Met Ala Lys Lys			
145		150	155
His Leu Glu Ile Asn Pro Glu His Pro Ile Val Glu Thr Leu Arg Gln			
165		170	175
Lys Ala Glu Ala Asp Lys Asn Asp Lys Ala Val Lys Asp Leu Val Val			
180		185	190
Leu Leu Phe Glu Thr Ala Leu Leu Ser Ser Gly Phe Ser Leu Asp Asp			
195		200	205
Pro Gln Thr His Ser Asn Arg Ile Tyr Arg Met Ile Lys Leu Gly Leu			
210		215	220
Gly Ile Asp Glu Asp Glu Pro Ala Ile Glu Glu Thr Thr Ala Ala Val			
225		230	235
Pro Asp Asp Ile Pro Pro Leu Glu Gly Glu Glu Asp Ala Ser Arg Met			
245		250	255
Glu Glu Val Asp			
260			